

# Supplementary Information

## Identification of New *N*-methyl-piperazine Chalcones as Dual MAO-B/AChE Inhibitors

Ashraf K. El-Damasy <sup>1,2,\*†</sup>, Jong Eun Park <sup>3,†</sup>, Hyun Ji Kim <sup>1</sup>, Jinhyuk Lee <sup>4,5</sup>, Eun-Kyoung Bang <sup>1</sup>, Hoon Kim <sup>3,\*</sup> and Gyochang Keum <sup>1,\*</sup>

<sup>1</sup> Center for Brain Technology, Brain Science Institute, Korea Institute of Science and Technology (KIST), Seoul 02792, Republic of Korea; hjkim926@kist.re.kr (H.J.K.); eunkbang@kist.re.kr (E.-K.B.)

<sup>2</sup> Department of Medicinal Chemistry, Faculty of Pharmacy, Mansoura University, Mansoura 35516, Egypt

<sup>3</sup> Department of Pharmacy, and Research Institute of Life Pharmaceutical Sciences, Suncheon National University, Suncheon 57922, Republic of Korea; park140201@naver.com

<sup>4</sup> Disease Target Structure Research Center, Korea Research Institute of Bioscience and Biotechnology (KRIBB), Daejeon 34141, Republic of Korea; jinhyuk@kribb.re.kr

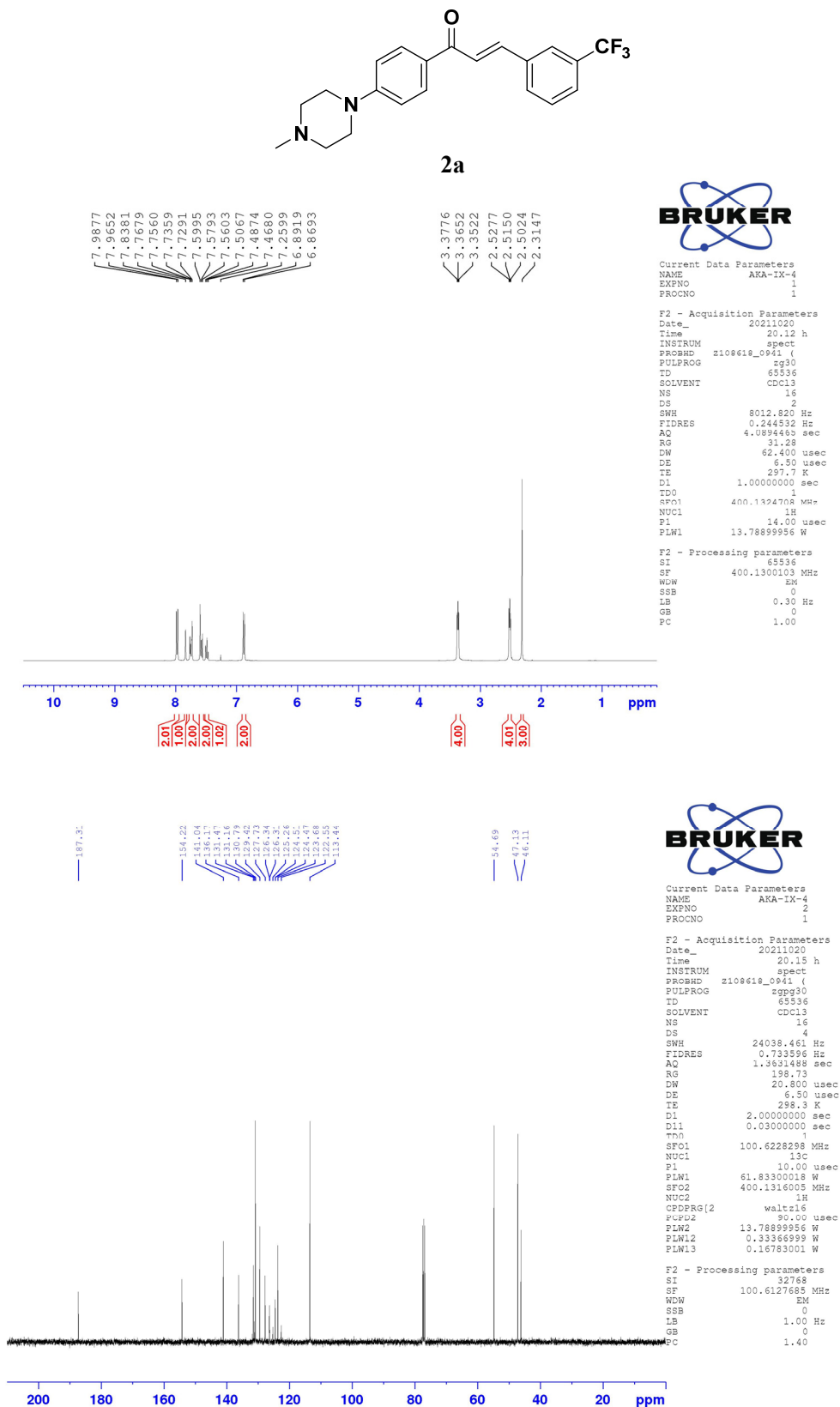
<sup>5</sup> Department of Bioinformatics, KRIBB School of Bioscience, University of Science and Technology (UST), Daejeon 34113, Republic of Korea

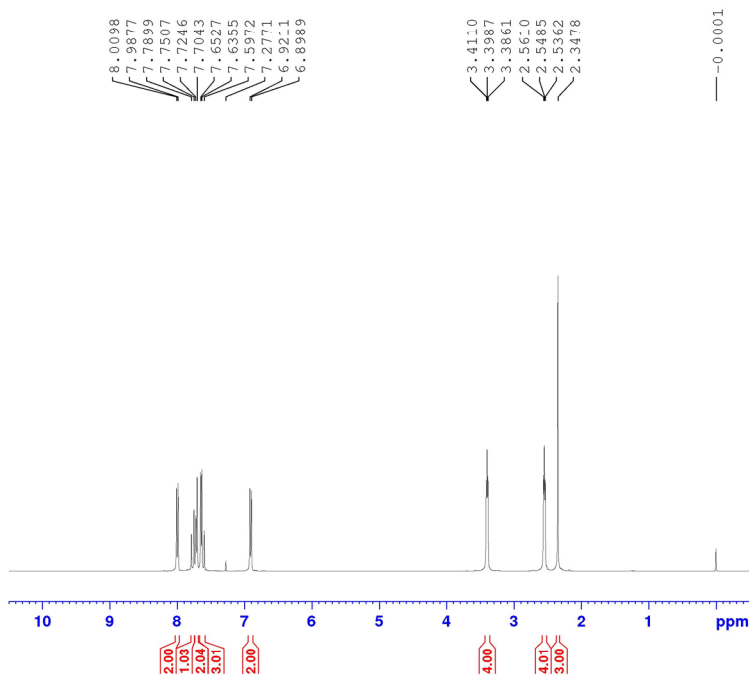
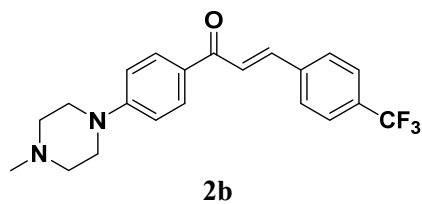
\* Correspondence: ashraf.el-damasy@kist.re.kr (A.K.E.-D.); hoon@sunchon.ac.kr (H.K.); gkeum@kist.re.kr (G.K.)

† These authors contributed equally to this work.

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Figure S1.  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra





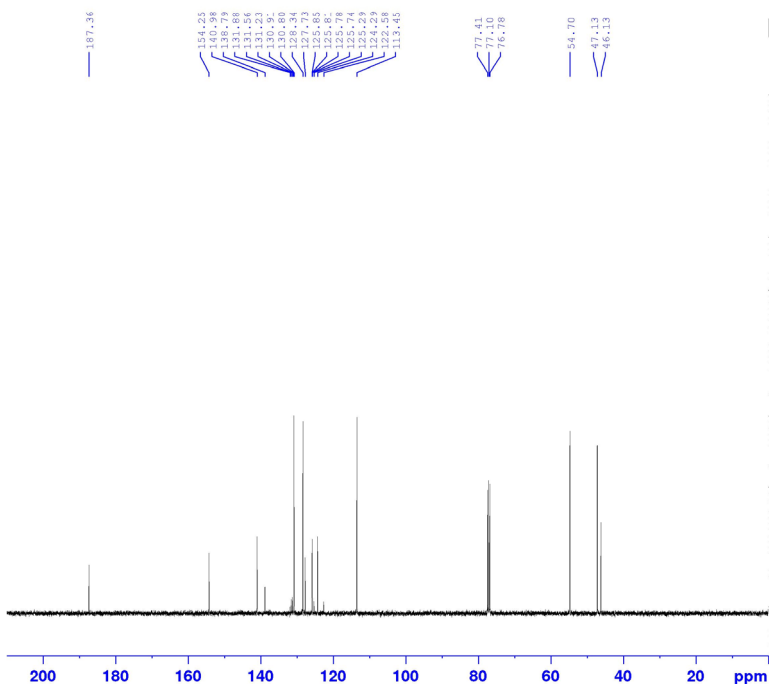
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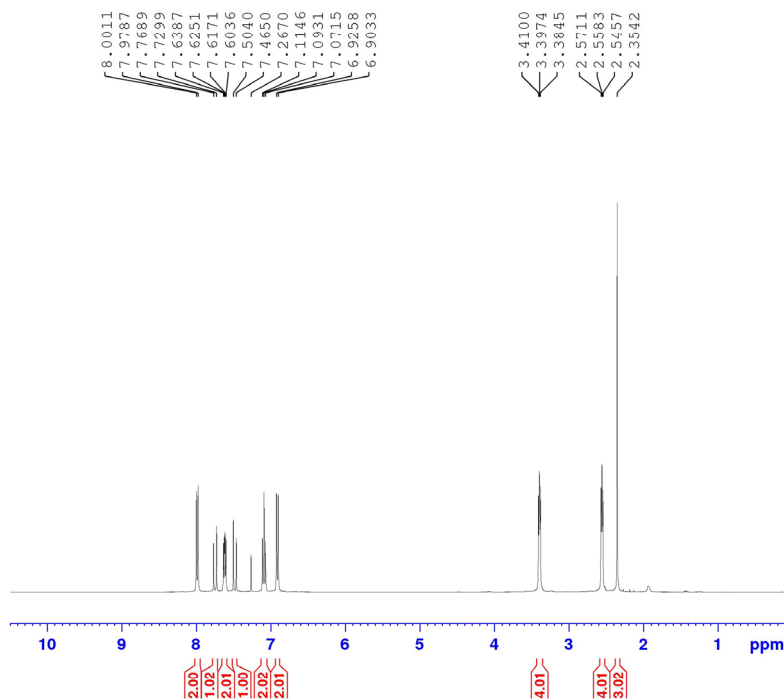
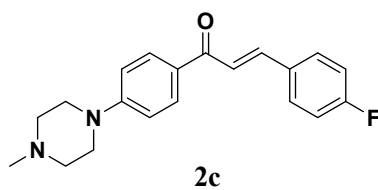
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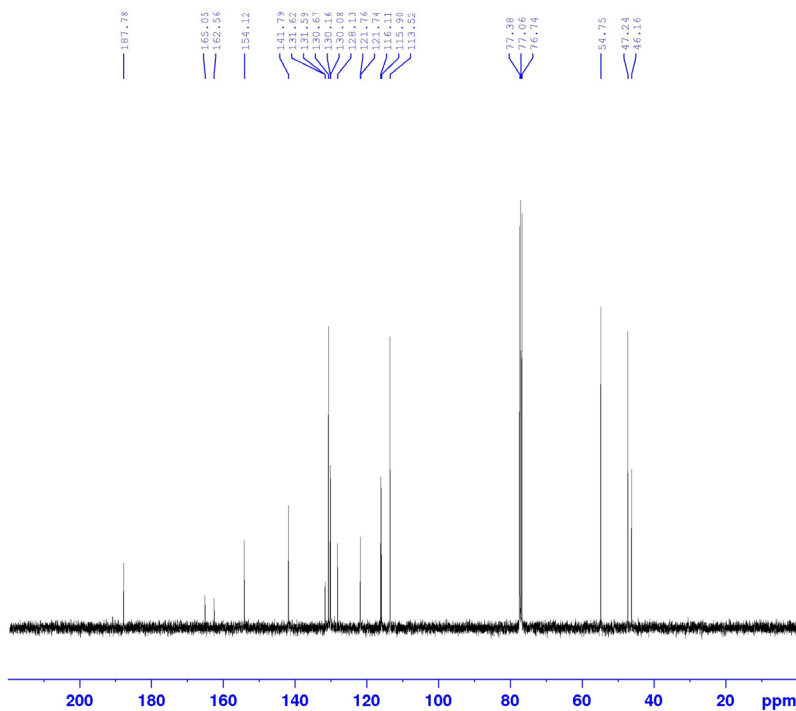


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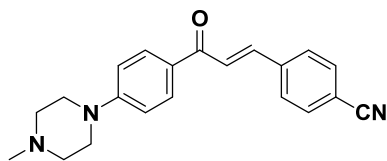
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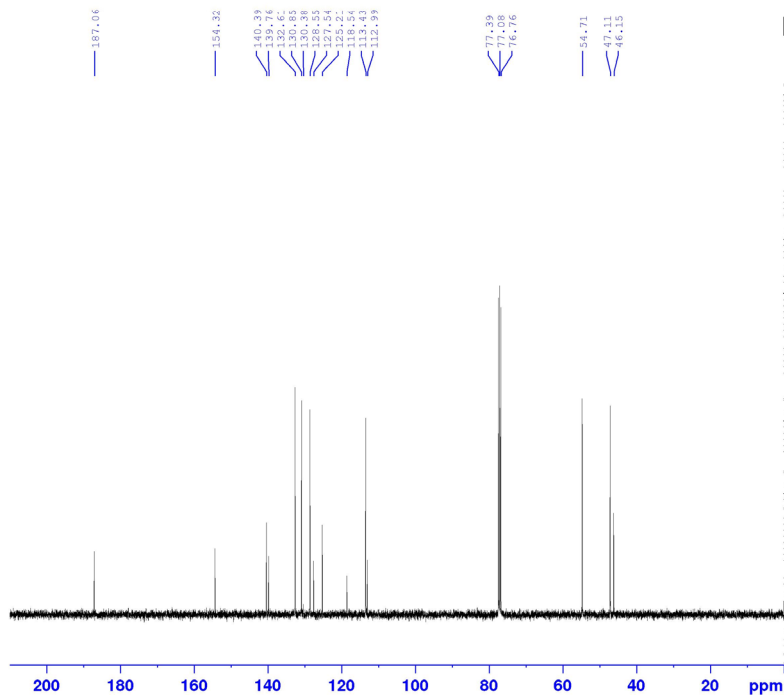
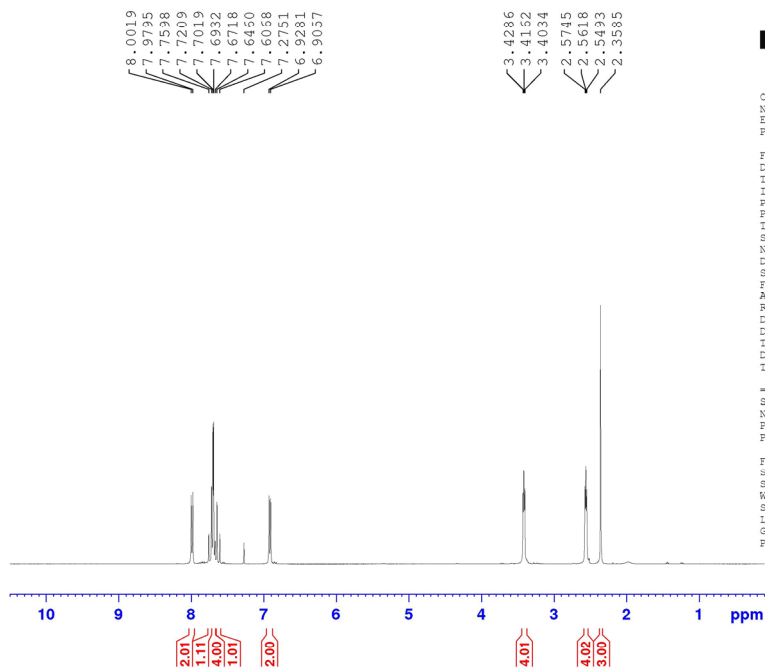
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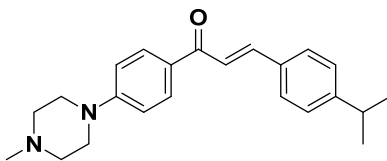
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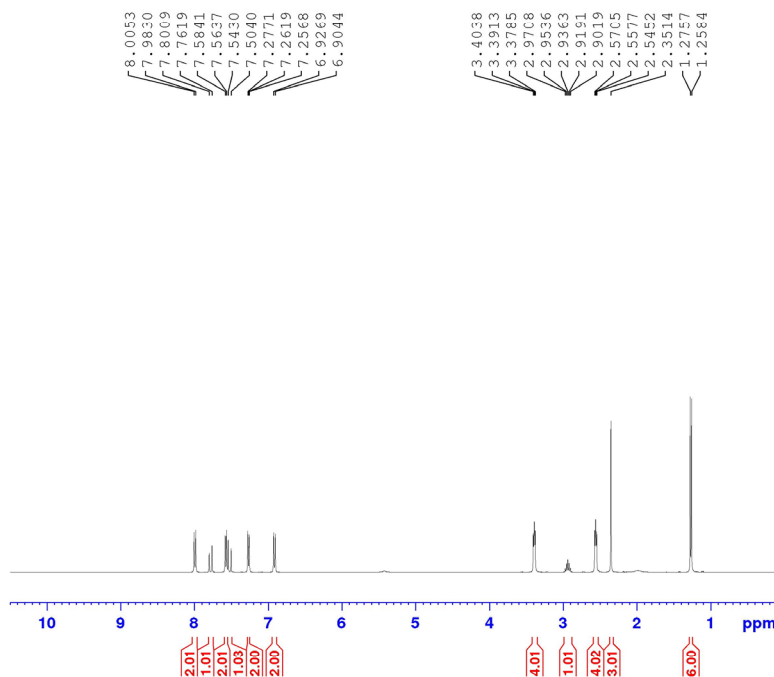


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2e

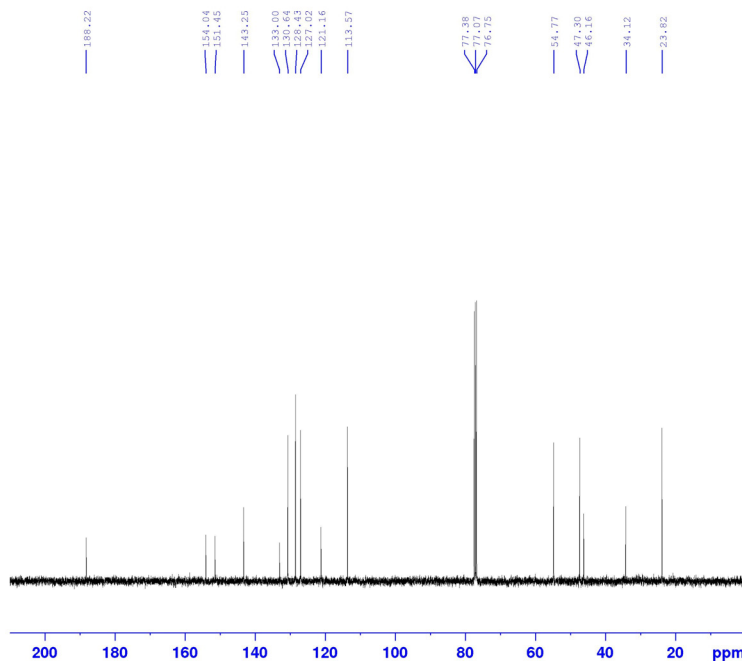


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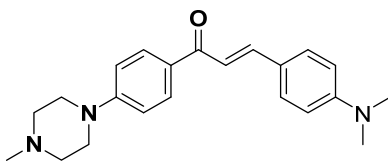
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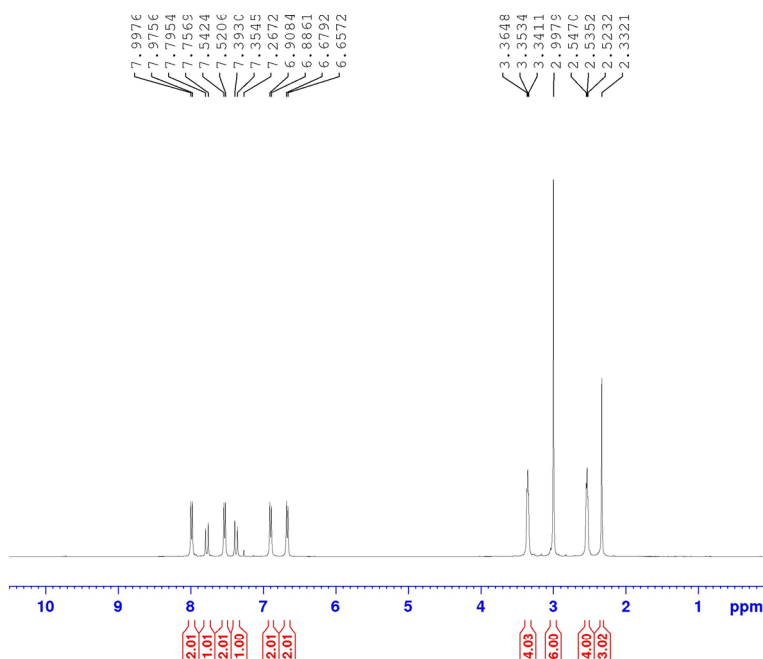
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2f

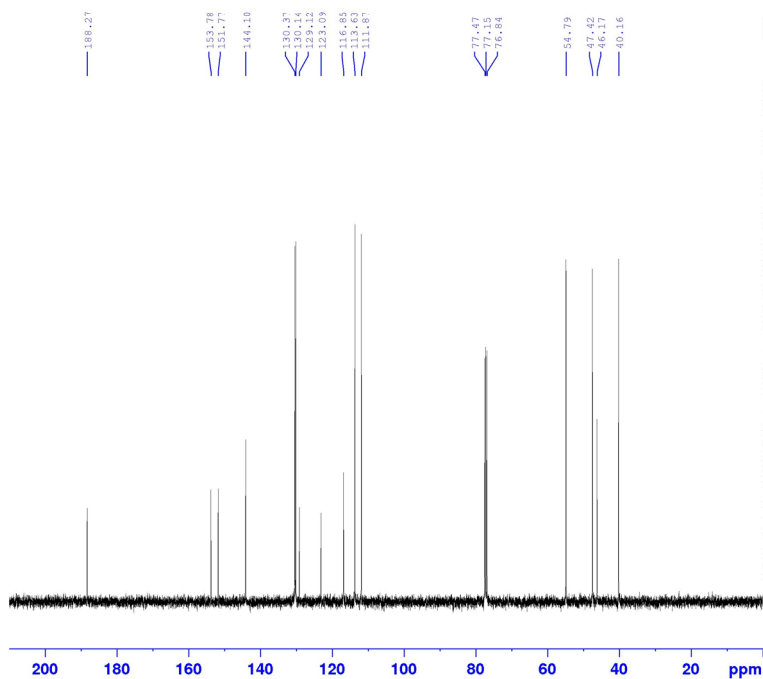


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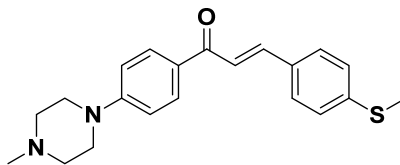
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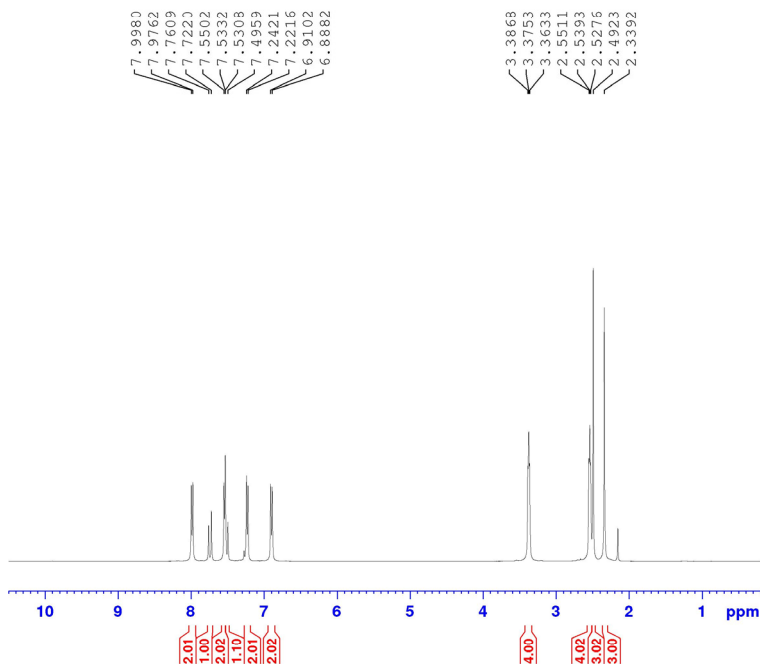
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2g

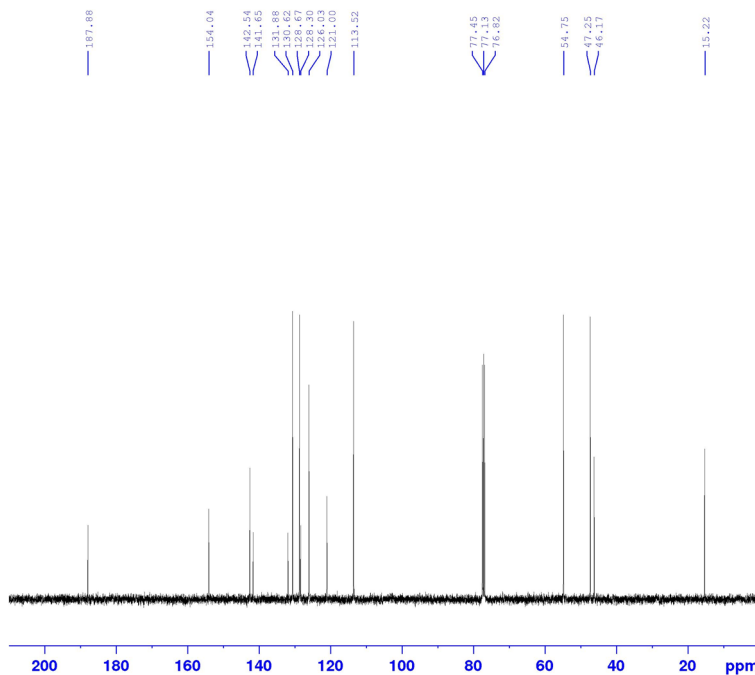


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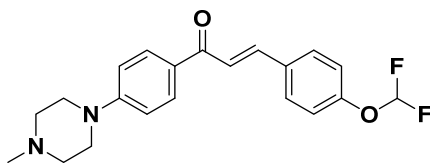
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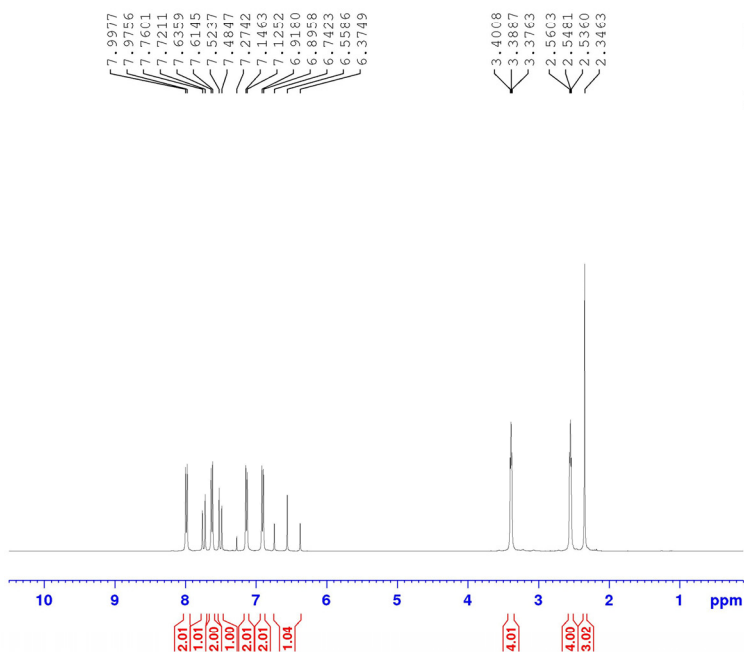
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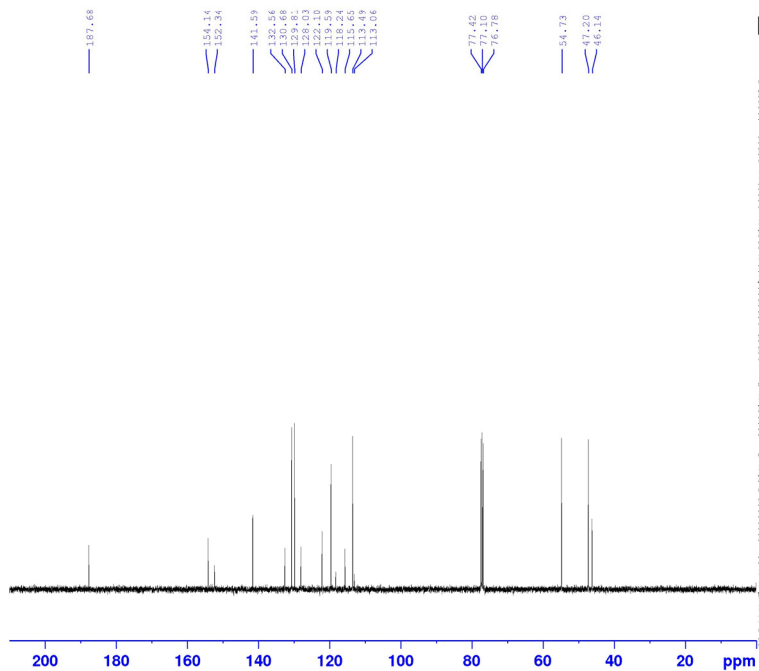
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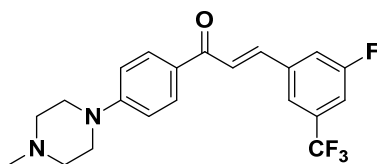
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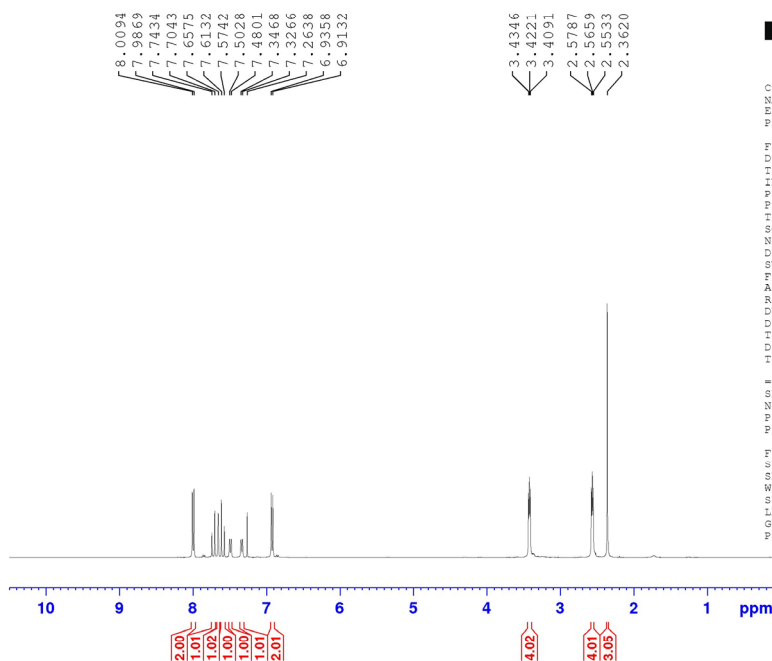
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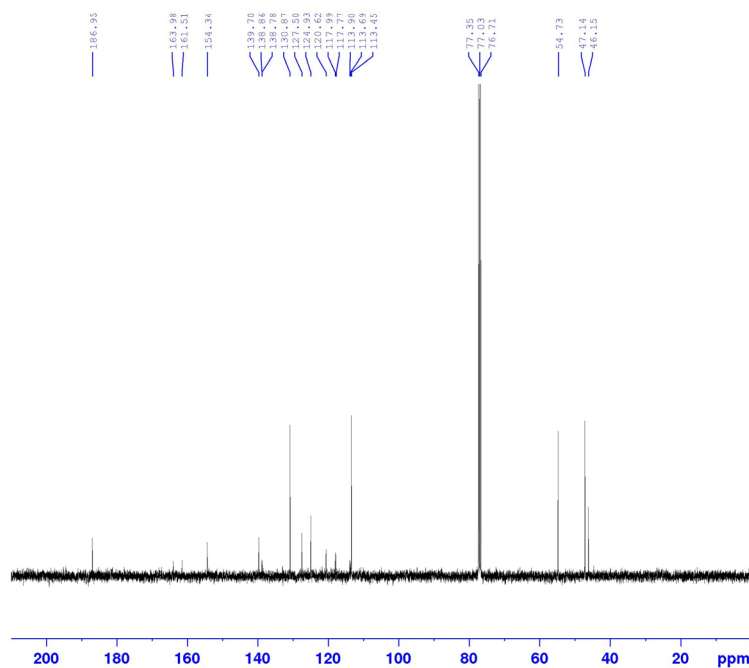


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TE 297.9 K  
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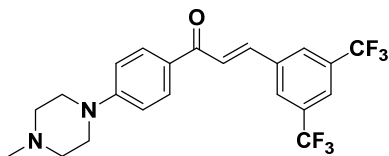
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FIDRES 0.366798 Hz  
AQ 1.3631488 sec  
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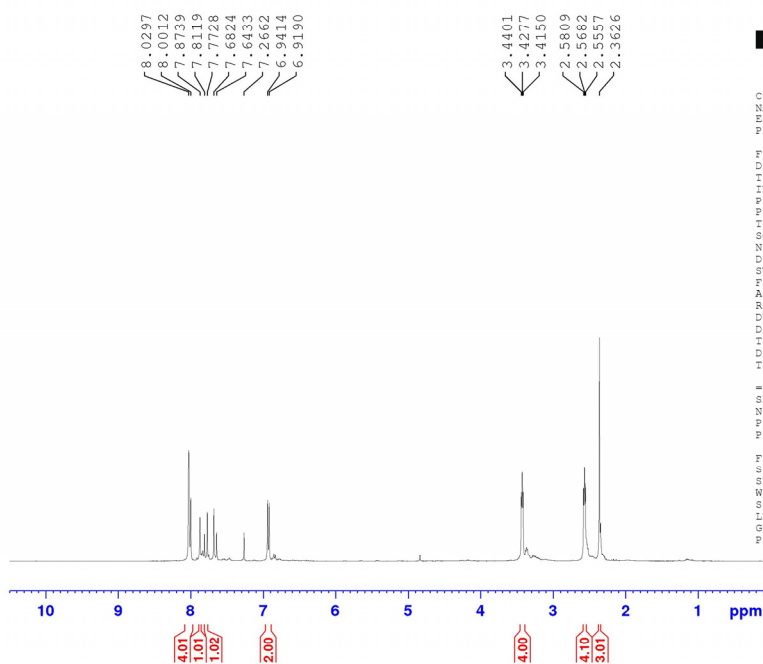
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2j

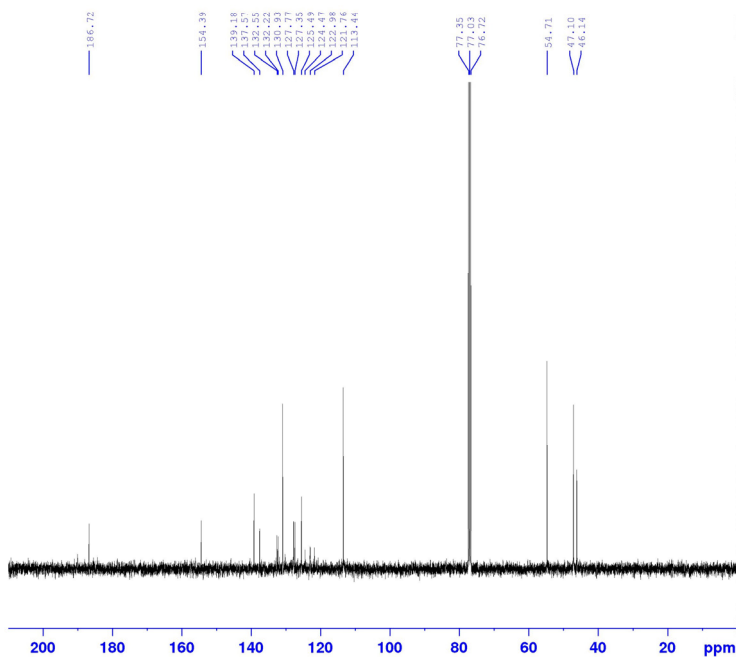


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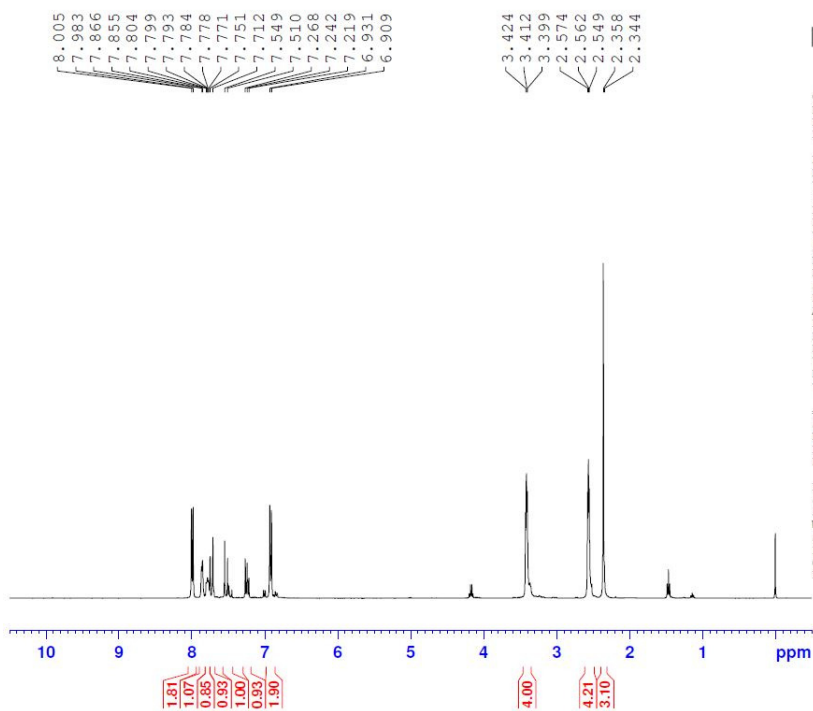
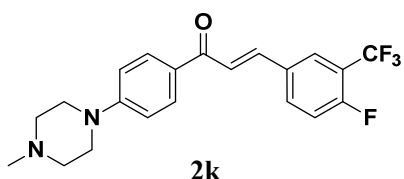
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SOLVENT CDCl<sub>3</sub>  
NS 100  
DS 4  
SWH 24038.461 Hz  
FIDRES 0.366798 Hz  
AQ 1.3633488 sec  
RG 190.62  
DW 20.800 usec  
DE 6.50 usec  
TE 298.9 K  
D1 2.00000000 sec  
D11 0.03000000 sec  
TDO 1

===== CHANNEL f1 =====  
SFO1 100.6428474 MHz  
NUC1 13C  
P1 10.00 usec  
PLW1 52.00000000 W

===== CHANNEL f2 =====  
SFO2 400.216008 MHz  
NUC2 1H  
CPDPRG2 waltz16  
PCPD2 90.00 usec  
PLW2 12.00000000 W  
PLW12 0.35777000 W  
PLW13 0.28979000 W

F2 - Processing parameters  
SI 32768  
SF 100.6328850 MHz  
WDW EM  
SSB 0  
LB 1.00 Hz  
GB 0  
PC 1.40

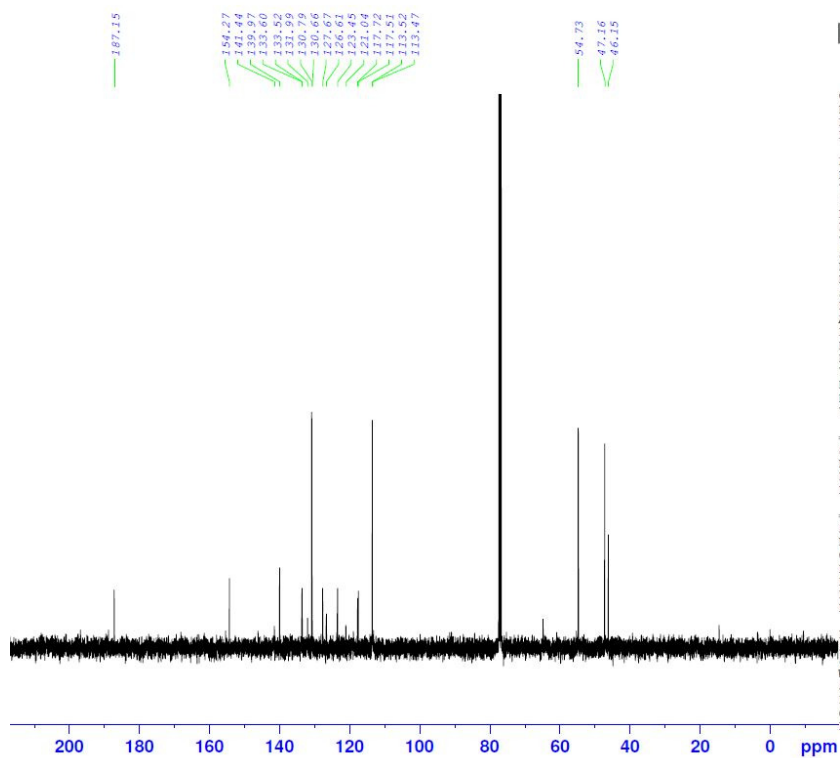


Current Data Parameters  
NAME AKA-VIII-27  
EXPNO 1  
PROCNO 1

F2 - Acquisition Parameters  
Date\_ 20210209  
Time 18.12  
INSTRUM spect  
PROBHD 5 mm PABBO BB/  
PULPROG zg30  
TD 65536  
SOLVENT CDCl<sub>3</sub>  
NS 5  
DS 2  
SWH 8012.820 Hz  
FIDRES 0.122266 Hz  
AQ 4.0894465 sec  
RG 91.91  
DW 62.400 usec  
DE 6.50 usec  
TE 298.2 K  
D1 1.00000000 sec  
TD0 1

===== CHANNEL f1 =====  
SFO1 400.2124715 MHz  
NUC1 1H  
P1 15.54 usec  
PLW1 12.00000000 W

F2 - Processing parameters  
SI 65536  
SF 400.2100100 MHz  
WDW EM  
SSB 0  
LB 0.30 Hz  
GB 0  
PC 1.00



Current Data Parameters  
NAME AKA-VIII-27  
EXPNO 2  
PROCNO 1

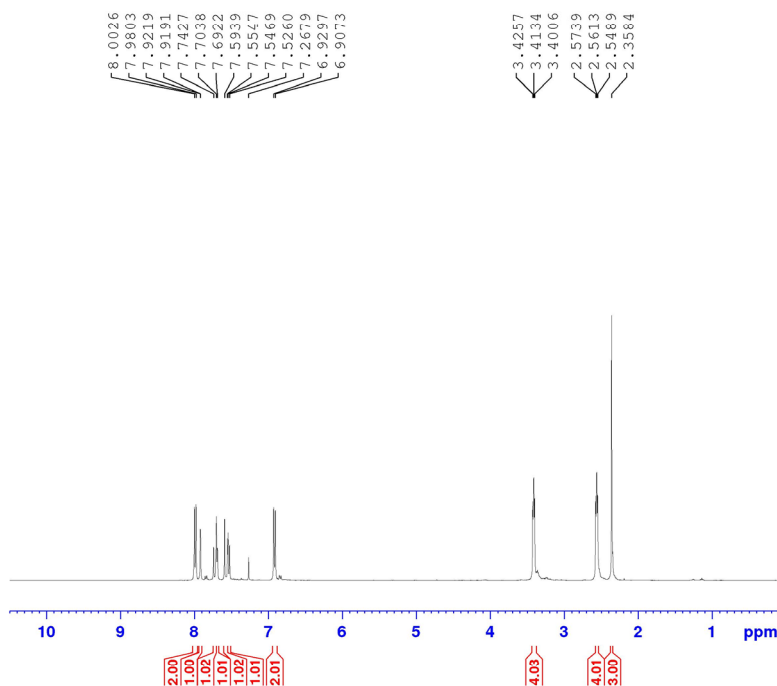
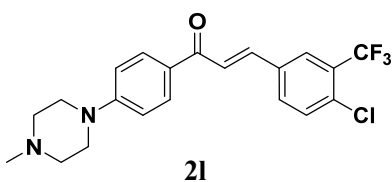
F2 - Acquisition Parameters  
Date\_ 20210209  
Time 18.16  
INSTRUM spect  
PROBHD 5 mm PABBO BB/  
PULPROG zgpg30  
TD 65536  
SOLVENT CDCl<sub>3</sub>  
NS 40  
DS 4  
SWH 24038.461 Hz  
FIDRES 0.366798 Hz  
AQ 1.3631488 sec  
RG 190.62  
DW 20.800 usec  
DE 6.50 usec  
TE 298.9 K  
D1 2.00000000 sec  
D11 0.03000000 sec  
TD0 1

===== CHANNEL f1 =====  
SFO1 100.6429474 MHz  
NUC1 13C  
P1 10.00 usec  
PLW1 52.00000000 W

===== CHANNEL f2 =====  
SFO2 400.2116008 MHz  
NUC2 1H  
CPDPRG2 waltz16  
PCPD2 90.00 usec  
PLW2 12.00000000 W  
PLW12 0.35777000 W  
PLW13 0.28979000 W

F2 - Processing parameters  
SI 32768  
SF 100.6328850 MHz  
WDW EM  
SSB 0  
LB 1.00 Hz  
GB 0  
PC 1.40



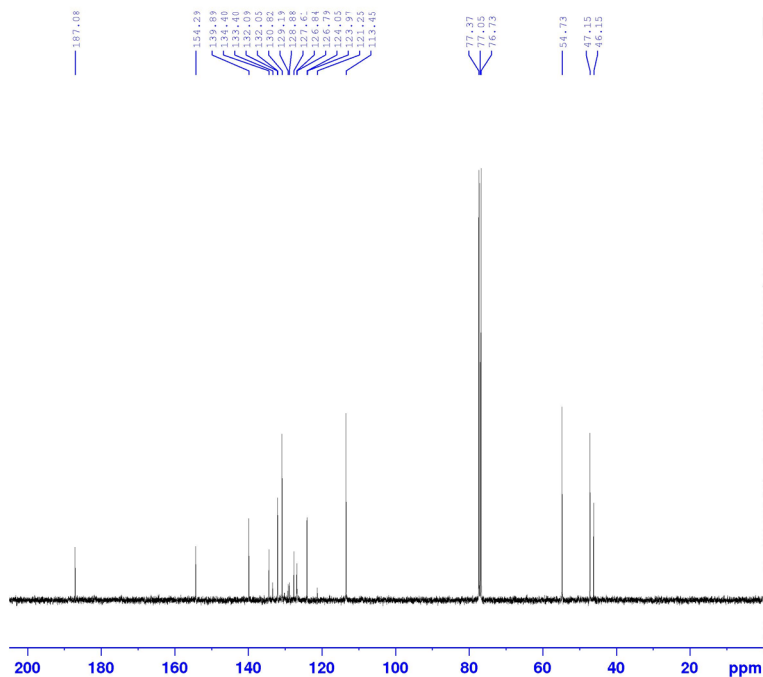


Current Data Parameters  
NAME AKA-VIII-28  
EXPNO 1  
PROCNO 1

F2 - Acquisition Parameters  
Date\_ 20210209  
Time 15.29  
INSTRUM spect  
PROBHD 5 mm PABBO BB/  
PULPROG zg30  
TD 65536  
SOLVENT CDCl3  
NS 16  
DS 2  
SWH 8012.520 Hz  
FIDRES 0.122266 Hz  
AQ 4.0894463 sec  
RG 103.95  
DW 62.400 usec  
DE 6.50 usec  
TE 297.6 K  
D1 1.00000000 sec  
TD0 1

===== CHANNEL f1 =====  
SFO1 400.2124715 MHz  
NUC1 1H  
P1 15.54 usec  
PLW1 12.00000000 W

F2 - Processing parameters  
SI 32768  
SF 400.2100098 MHz  
WDW EM  
SSB 0  
LB 0.30 Hz  
GB 0  
PC 1.00



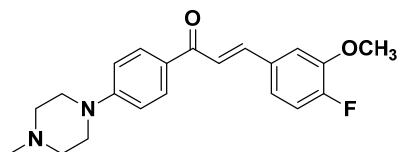
Current Data Parameters  
NAME AKA-VIII-28  
EXPNO 2  
PROCNO 1

F2 - Acquisition Parameters  
Date\_ 20210209  
Time 15.42  
INSTRUM spect  
PROBHD 5 mm PABBO BB/  
PULPROG zgpg30  
TD 65536  
SOLVENT CDCl3  
NS 200  
DS 4  
SWH 24038.461 Hz  
FIDRES 0.366798 Hz  
AQ 1.3631488 sec  
RG 190.62  
DW 20.800 usec  
DE 6.50 usec  
TE 298.4 K  
D1 2.00000000 sec  
D11 0.03000000 sec  
TD0 1

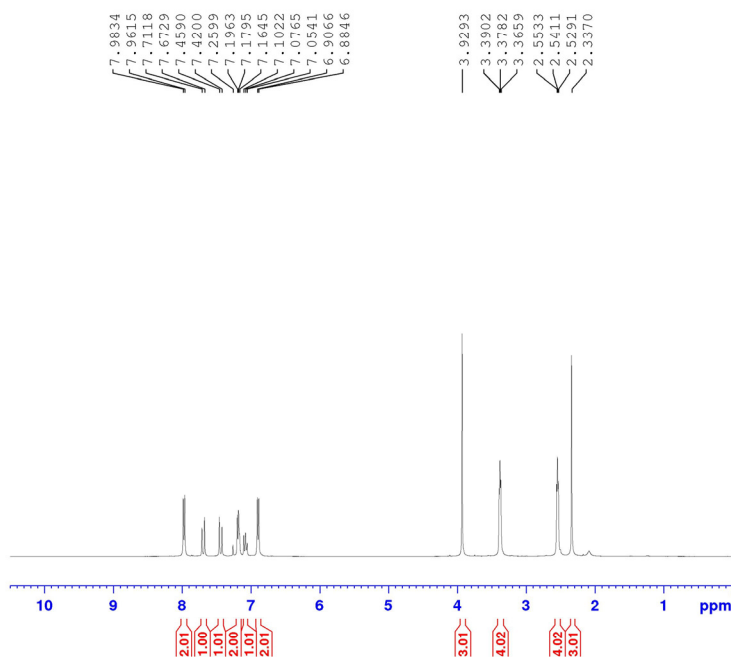
===== CHANNEL f1 =====  
SFO1 100.6429474 MHz  
NUC1 13C  
P1 10.00 usec  
PLW1 52.00000000 W

===== CHANNEL f2 =====  
SFO2 400.2116008 MHz  
NUC2 1H  
CPDPRG[2] waltz16  
PCPD2 90.00 usec  
PLW2 12.00000000 W  
PLW12 0.35777000 W  
PLW13 0.28979000 W

F2 - Processing parameters  
SI 32768  
SF 100.6328850 MHz  
WDW EM  
SSB 0  
LB 1.00 Hz  
GB 0  
PC 1.40



2m

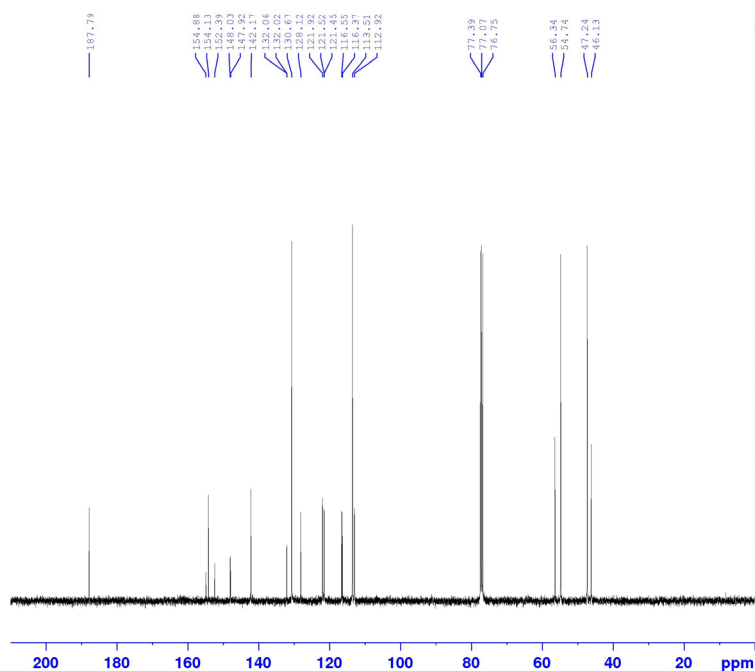


Current Data Parameters  
NAME AK-Vill-30  
EXPNO 1  
PROCNO 1

F2 - Acquisition Parameters  
Date\_ 20220809  
Time 11.52  
INSTRUM spect  
PROBHD 5 mm PABBO BB/  
PULPROG zg30  
TD 65536  
SOLVENT CDCl3  
NS 16  
DS 2  
SWH 8012.820 Hz  
FIDRES 0.122266 Hz  
AQ 4.0894465 sec  
RG 76.56  
DW 62.400 usec  
DE 6.50 usec  
TE 300.0 K  
D1 1.00000000 sec  
TDO 1

===== CHANNEL f1 =====  
SFO1 400.2124715 MHz  
NUC1 1H  
P1 16.00 usec  
PLW1 13.00000000 W

F2 - Processing parameters  
SI 65536  
SF 400.2100131 MHz  
WDW EM  
SSB 0  
LB 0.30 Hz  
GB 0  
PC 1.00



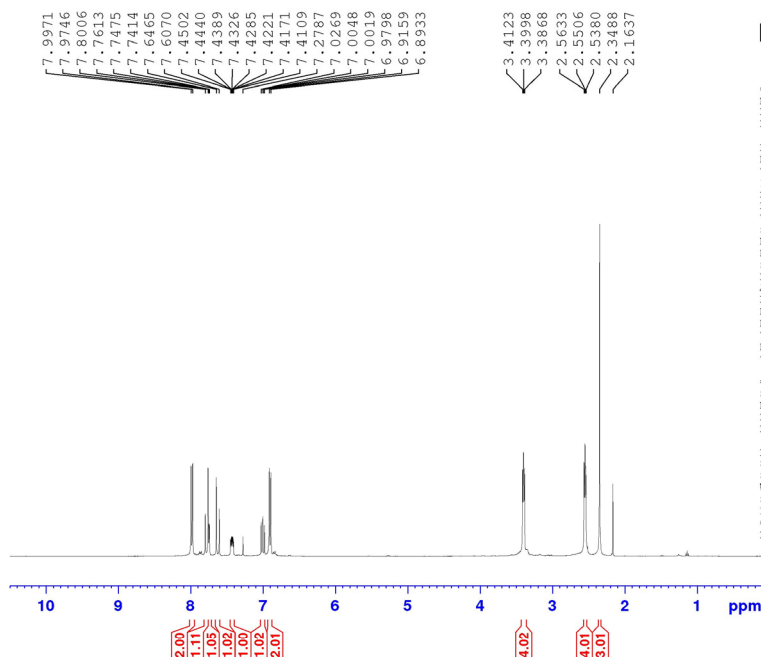
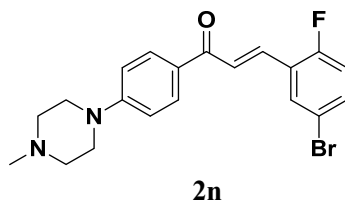
Current Data Parameters  
NAME AK-Vill-30  
EXPNO 2  
PROCNO 1

F2 - Acquisition Parameters  
Date\_ 20220809  
Time 11.55  
INSTRUM spect  
PROBHD 5 mm PABBO BB/  
PULPROG zgpg30  
TD 65536  
SOLVENT CDCl3  
NS 300  
DS 4  
SWH 24038.461 Hz  
FIDRES 0.366798 Hz  
AQ 1.3631488 sec  
RG 190.62  
DW 20.800 usec  
DE 6.50 usec  
TE 300.6 K  
D1 2.00000000 sec  
D11 0.03000000 sec  
TDO 1

===== CHANNEL f1 =====  
SFO1 100.6429474 MHz  
NUC1 13C  
P1 10.00 usec  
PLW1 65.00000000 W

===== CHANNEL f2 =====  
SFO2 400.2116008 MHz  
NUC2 1H  
CPDPRG2 waltz16  
PCPD2 90.00 usec  
PLW2 13.00000000 W  
PLW12 0.36111000 W  
PLW13 0.29249999 W

F2 - Processing parameters  
SI 32768  
SF 100.6328850 MHz  
WDW EM  
SSB 0  
LB 1.00 Hz  
GB 0  
PC 1.40

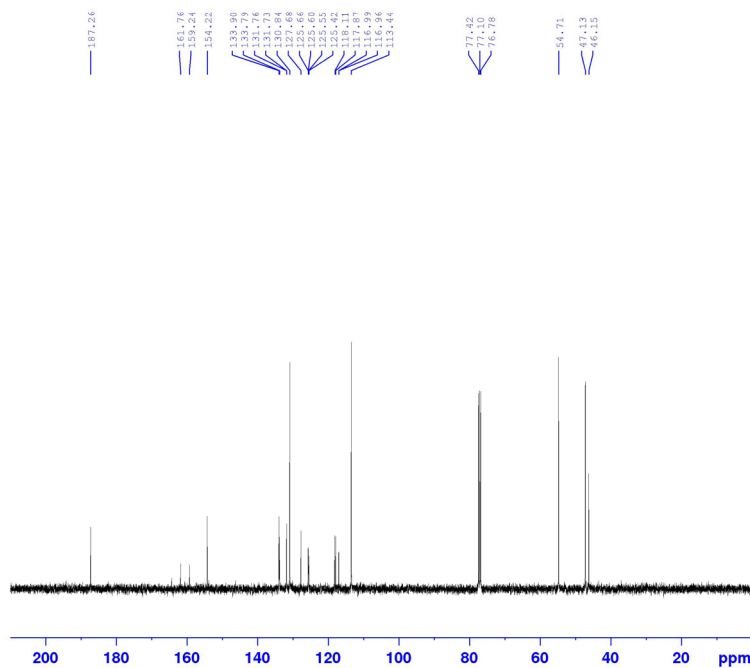


Current Data Parameters  
NAME AKA-VIII-94  
EXPNO 1  
PROCNO 1

F2 - Acquisition Parameters  
Date\_ 20211020  
Time 19:41  
INSTRUM spect  
PROBHD 5 mm PABBO BB/  
PULPROG zg30  
TD 65536  
SOLVENT CDCl<sub>3</sub>  
NS 16  
DS 2  
SWH 8012.820 Hz  
FIDRES 0.122266 Hz  
AQ 4.0894465 sec  
RG 38.64  
DW 62.400 usec  
DE 6.50 usec  
TE 295.8 K  
D1 1.00000000 sec  
TD0 1

===== CHANNEL f1 =====  
SFO1 400.2124715 MHz  
NUC1 1H  
P1 16.00 usec  
PLW1 13.00000000 W

F2 - Processing parameters  
SI 65536  
SF 400.2100054 MHz  
WDW EM  
SSB 0  
LB 0.30 Hz  
GB 0  
PC 1.00



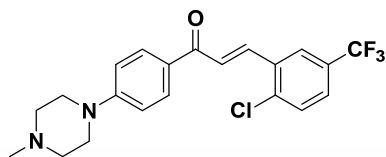
Current Data Parameters  
NAME AKA-VIII-94  
EXPNO 2  
PROCNO 1

F2 - Acquisition Parameters  
Date\_ 20211020  
Time 19:45  
INSTRUM spect  
PROBHD 5 mm PABBO BB/  
PULPROG zgpg30  
TD 65536  
SOLVENT CDCl<sub>3</sub>  
NS 40  
DS 4  
SWH 24038.461 Hz  
FIDRES 0.366798 Hz  
AQ 1.3631488 sec  
RG 190.62  
DW 20.800 usec  
DE 6.50 usec  
TE 297.5 K  
D1 2.00000000 sec  
D11 0.03000000 sec  
TD0 1

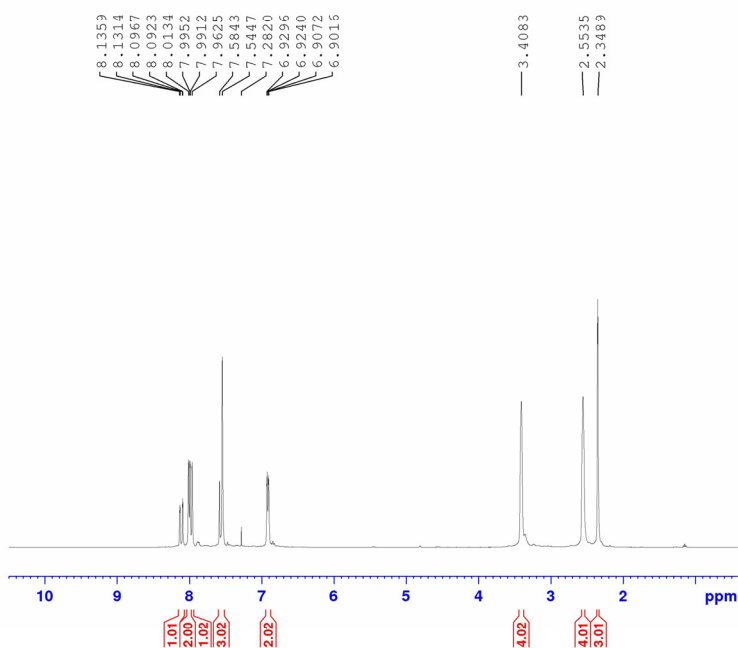
===== CHANNEL f1 =====  
SFO1 100.6429474 MHz  
NUC1 13C  
P1 10.00 usec  
PLW1 65.00000000 W

===== CHANNEL f2 =====  
SFO2 400.2116008 MHz  
NUC2 1H  
CPDPRG2 waltz16  
PCPD2 30.00 usec  
PLW2 13.00000000 W  
PLW12 0.36111000 W  
PLW13 0.29249999 W

F2 - Processing parameters  
SI 32768  
SF 100.6328850 MHz  
WDW EM  
SSB 0  
LB 1.00 Hz  
GB 0  
PC 1.40



2o

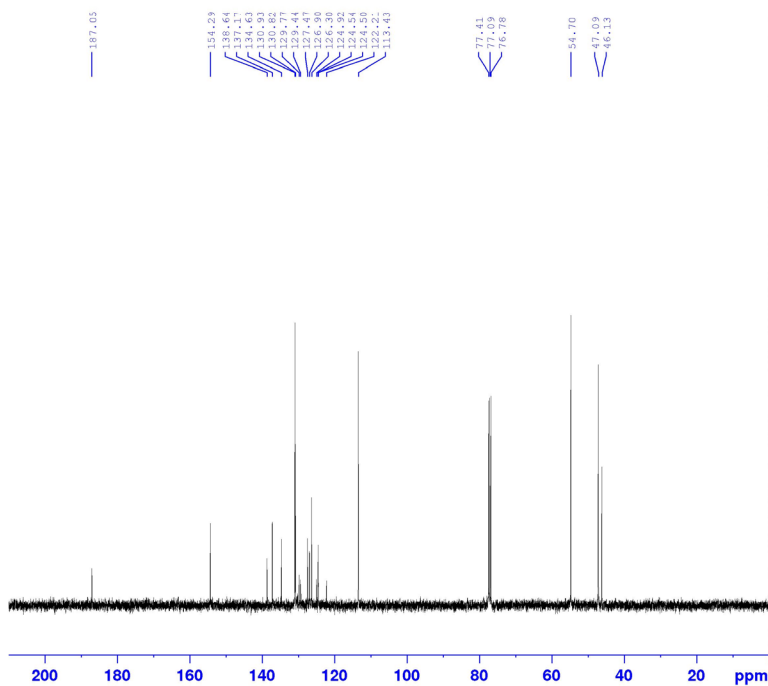


Current Data Parameters  
NAME AKA-IX-1  
EXPNO 1  
PROCNO 1

F2 - Acquisition Parameters  
Date\_ 20211020  
Time 19.52  
INSTRUM spect  
PROBHD 5 mm PABBO BB/  
PULPROG zg30  
TD 65536  
SOLVENT CDCl<sub>3</sub>  
NS 16  
DS 2  
SWH 8012.820 Hz  
FIDRES 0.122266 Hz  
AQ 4.0894465 sec  
RG 52.97  
DM 62.400 usec  
DE 6.50 usec  
TE 298.9 K  
D1 1.00000000 sec  
TD0 1

===== CHANNEL f1 =====  
SFO1 400.2124715 MHz  
NUC1 1H  
P1 16.00 usec  
PLW1 13.00000000 W

F2 - Processing parameters  
SI 65536  
SF 400.2100041 MHz  
WDW EM  
SSB 0  
LB 0.30 Hz  
GB 0  
PC 1.00



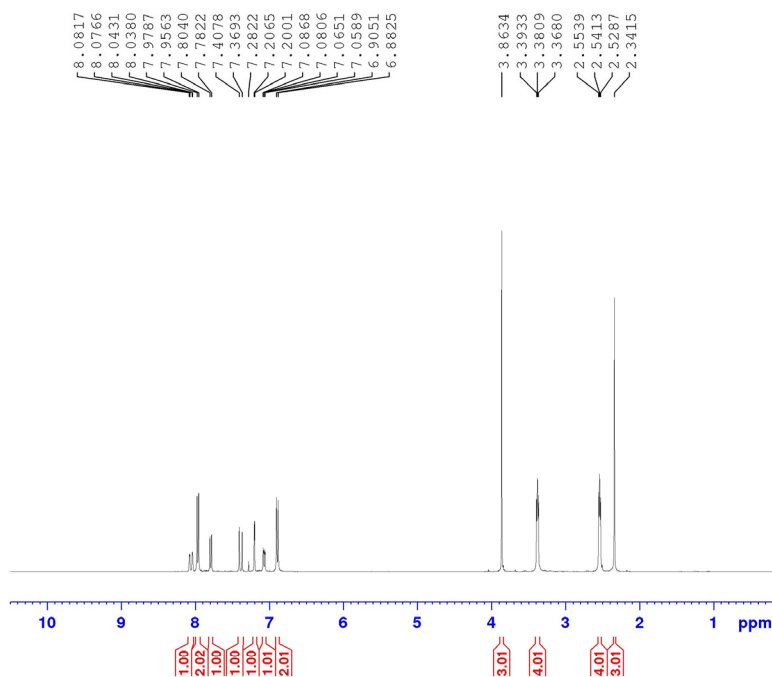
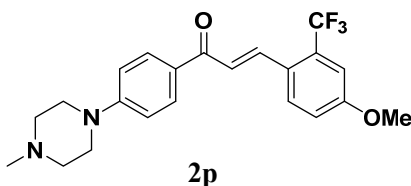
Current Data Parameters  
NAME AKA-IX-1  
EXPNO 2  
PROCNO 1

F2 - Acquisition Parameters  
Date\_ 20211020  
Time 19.56  
INSTRUM spect  
PROBHD 5 mm PABBO BB/  
PULPROG zgpg30  
TD 65536  
SOLVENT CDCl<sub>3</sub>  
NS 40  
DS 4  
SWH 24038.461 Hz  
FIDRES 0.366798 Hz  
AQ 1.3631488 sec  
RG 190.62  
DM 20.800 usec  
DE 6.50 usec  
TE 297.6 K  
D1 2.00000000 sec  
D11 0.03000000 sec  
TD0 1

===== CHANNEL f1 =====  
SFO1 100.6429474 MHz  
NUC1 13C  
P1 10.00 usec  
PLW1 65.00000000 W

===== CHANNEL f2 =====  
SFO2 400.2116008 MHz  
NUC2 1H  
CPDPRG2 waltz16  
PCPD2 90.00 usec  
PLW2 13.00000000 W  
PLW12 0.36111000 W  
PLW13 0.29249999 W

F2 - Processing parameters  
SI 32768  
SF 100.6328850 MHz  
WDW EM  
SSB 0  
LB 1.00 Hz  
GB 0  
PC 1.40

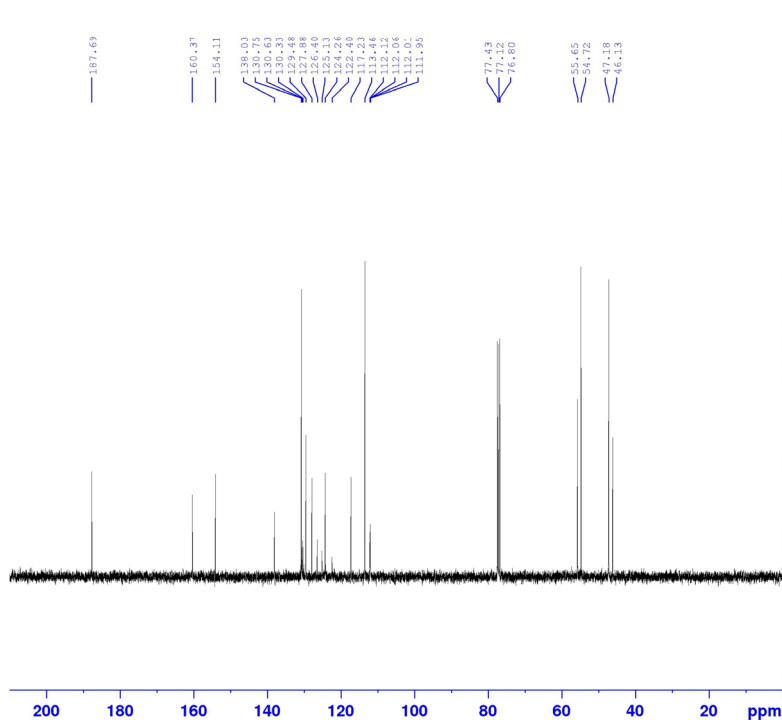


Current Data Parameters  
NAME AKA-IX-3  
EXPNO 1  
PROCNO 1

F2 - Acquisition Parameters  
Date\_ 20211021  
Time 13.01  
INSTRUM spect  
PROBHD 5 mm PABBO sb/  
PULPROG zg30  
TD 65536  
SOLVENT CDCl3  
NS 16  
DS 2  
SWH 8012.820 Hz  
FIDRES 0.122266 Hz  
AQ 4.0894465 sec  
RG 33.2  
DM 62.400 usec  
DE 6.50 usec  
TE 296.9 K  
D1 1.00000000 sec  
TD0 1

===== CHANNEL f1 =====  
SF01 400.2124715 MHz  
NUC1 1H  
P1 16.00 usec  
PLW1 13.00000000 W

F2 - Processing parameters  
SI 65536  
SF 400.2100040 MHz  
WDW EM  
SSB 0  
LB 0.30 Hz  
GB 0  
PC 1.00



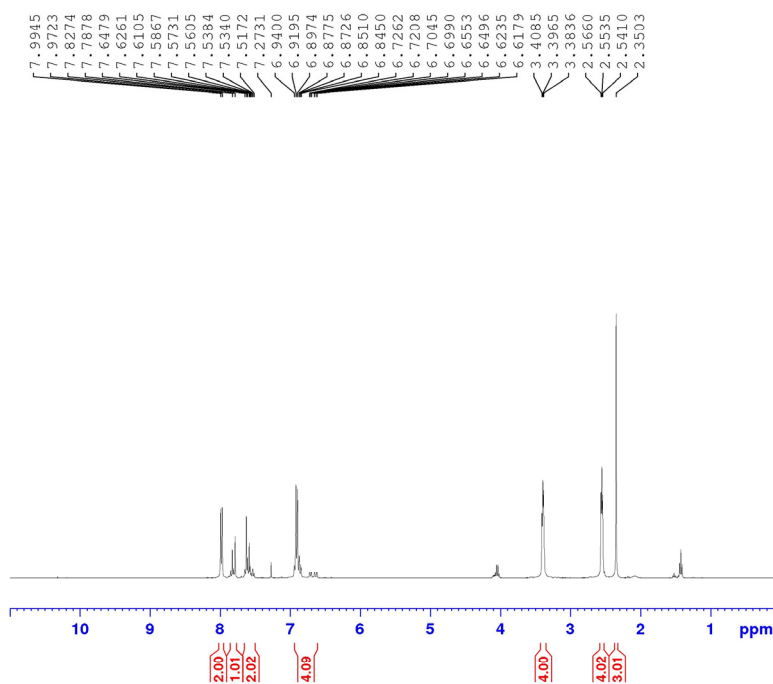
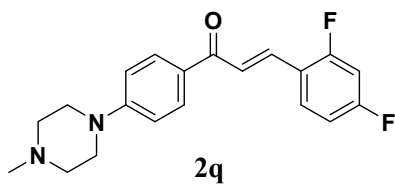
Current Data Parameters  
NAME AKA-IX-3  
EXPNO 2  
PROCNO 1

F2 - Acquisition Parameters  
Date\_ 20211021  
Time 13.03  
INSTRUM spect  
PROBHD 5 mm PABBO sb/  
PULPROG zgpg30  
TD 65536  
SOLVENT CDCl3  
NS 20  
DS 4  
SWH 24038.461 Hz  
FIDRES 0.366798 Hz  
AQ 1.5631488 sec  
RG 190.62  
DM 20.800 usec  
DE 6.50 usec  
TE 297.4 K  
D1 2.00000000 sec  
D11 0.03000000 sec  
TD0 1

===== CHANNEL f1 =====  
SF01 100.6429474 MHz  
NUC1 13C  
P1 10.00 usec  
PLW1 65.00000000 W

===== CHANNEL f2 =====  
SF02 400.2116008 MHz  
NUC2 1H  
CPDPRG2 waltz16  
PCPD2 90.00 usec  
PLW2 13.00000000 W  
PLW12 0.36111000 W  
PLW13 0.29249999 W

F2 - Processing parameters  
SI 32768  
SF 100.6328850 MHz  
WDW EM  
SSB 0  
LB 1.00 Hz  
GB 0  
PC 1.40



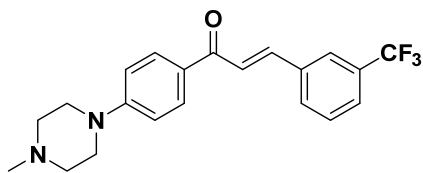
Current Data Parameters  
NAME AKA-IX-17  
EXPNO 1  
PROCNO 1

F2 - Acquisition Parameters  
Date\_ 20211114  
Time 21.46  
INSTRUM spect  
PROBHD 5 mm PABBO ss/  
PULPROG zg30  
TD 65536  
SOLVENT CDCl3  
NS 8  
DS 2  
SWH 8012.820 Hz  
FIDRES 0.122266 Hz  
AQ 4.0894465 sec  
RG 69.69  
DW 62.400 usec  
DE 6.50 usec  
TE 297.7 K  
D1 1.00000000 sec  
TDO 1

===== CHANNEL f1 =====  
SFO1 400.2124715 MHz  
NUC1 1H  
P1 16.00 usec  
PLW1 13.00000000 W

F2 - Processing parameters  
SI 65536  
SF 400.2100076 MHz  
WDW EM  
SSB 0  
LB 0.30 Hz  
GB 0  
PC 1.00

Figure S2. HRMS charts



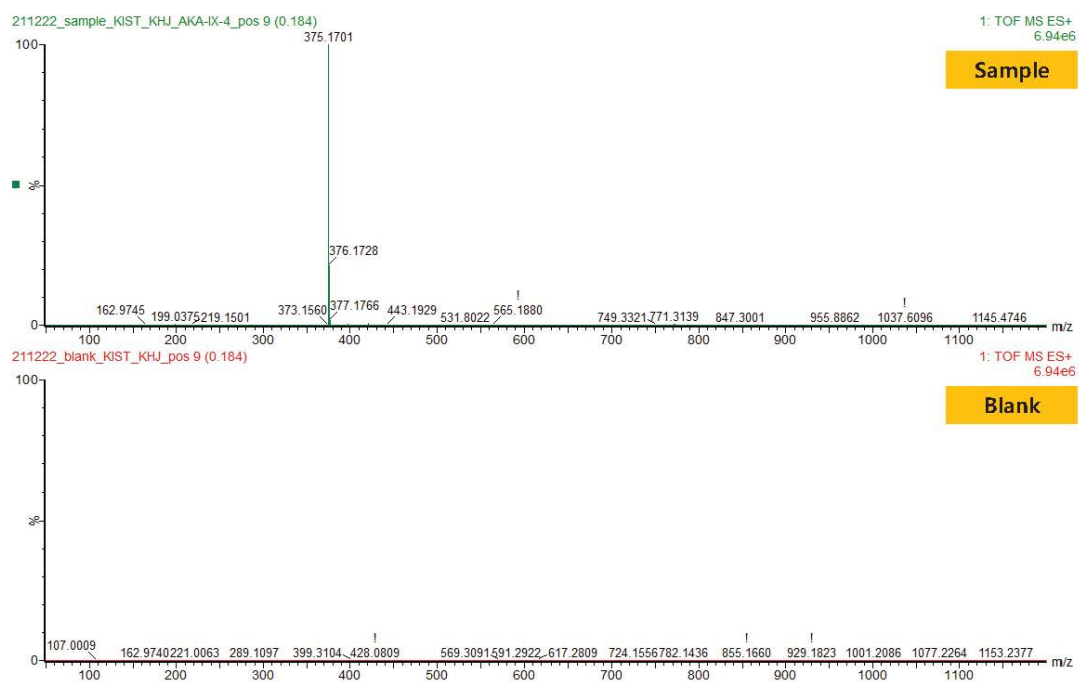
**2a**

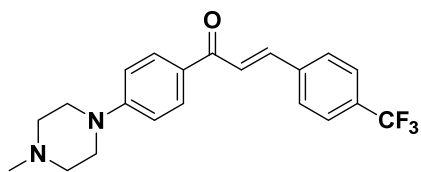
$\text{C}_{21}\text{H}_{22}\text{F}_3\text{N}_2\text{O} [\text{M}+\text{H}]^+$ :

Calculated: 375.1684

Found: 375.1701

Mass Spectrum: AKA-IX-4 (Positive mode)





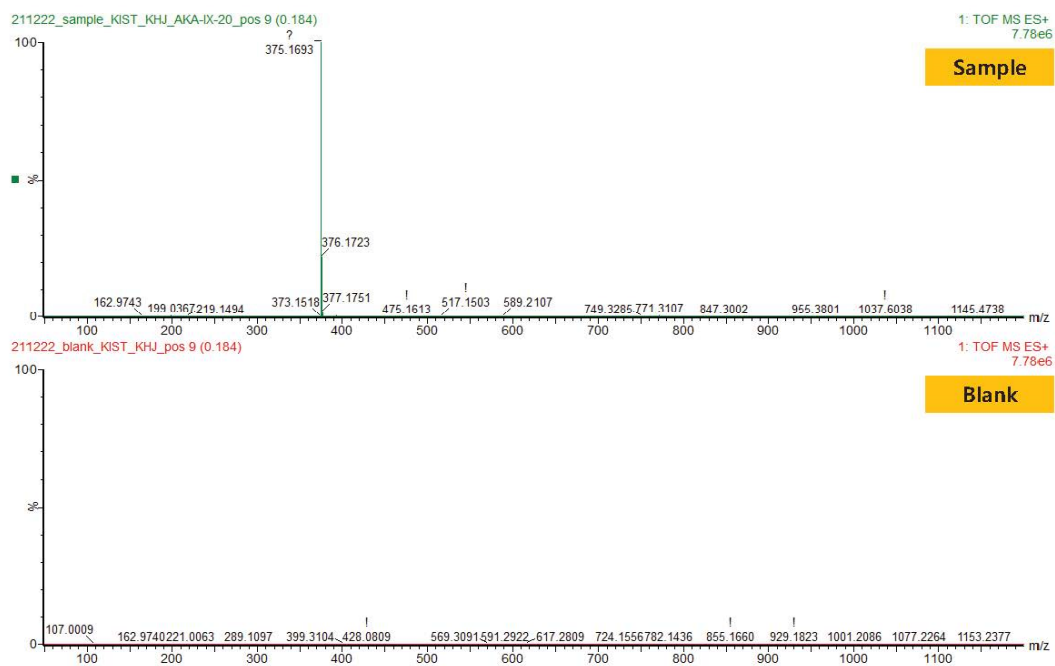
**2b**

$\text{C}_{21}\text{H}_{22}\text{F}_3\text{N}_2\text{O}$   $[\text{M}+\text{H}]^+$ :

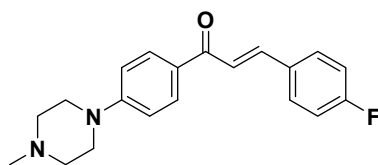
Calculated: 375.1684

Found: 375.1693

### Mass Spectrum: AKA-IX-20 (Positive mode)







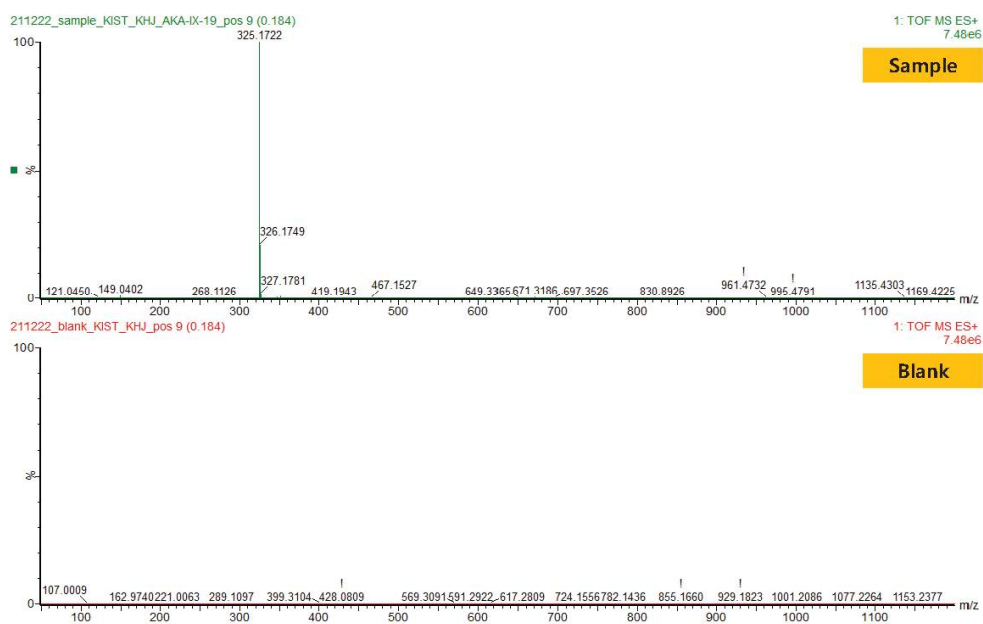
**2c**

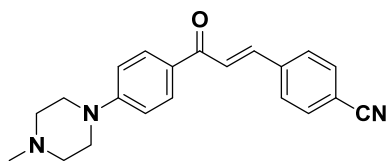
$\text{C}_{20}\text{H}_{22}\text{FN}_2\text{O}$   $[\text{M}+\text{H}]^+$ :

Calculated: 325.1716

Found: 325.1722

### Mass Spectrum: AKA-IX-19 (Positive mode)





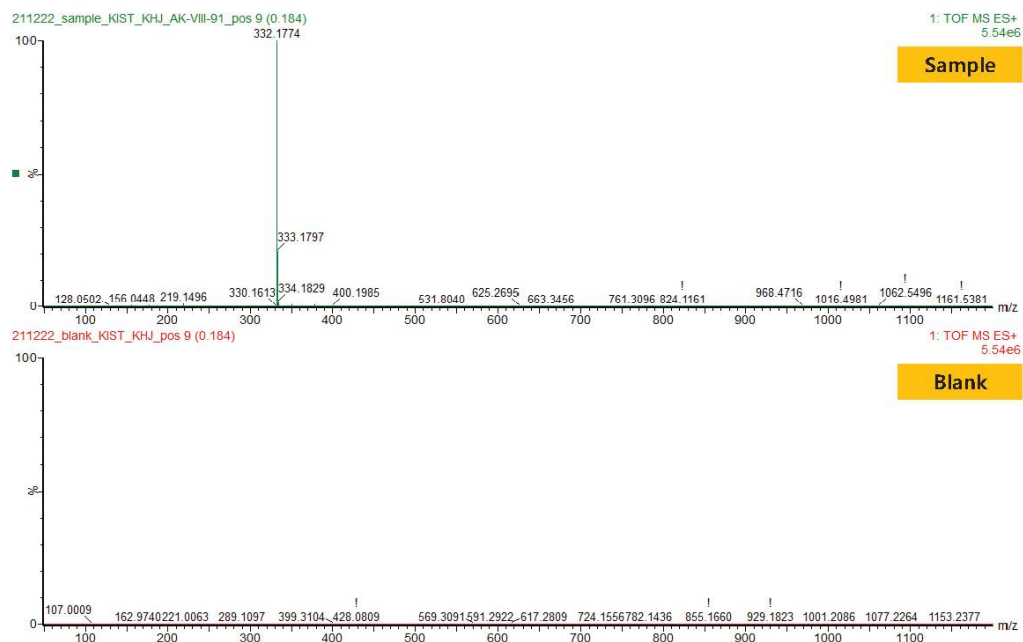
**2d**

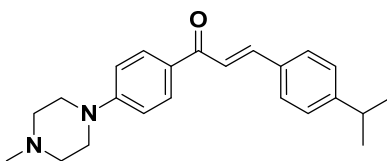
$\text{C}_{21}\text{H}_{22}\text{N}_3\text{O}$   $[\text{M}+\text{H}]^+$ :

Calculated: 332.1763

Found: 332.1774

### Mass Spectrum: AK-VIII-91 (Positive mode)





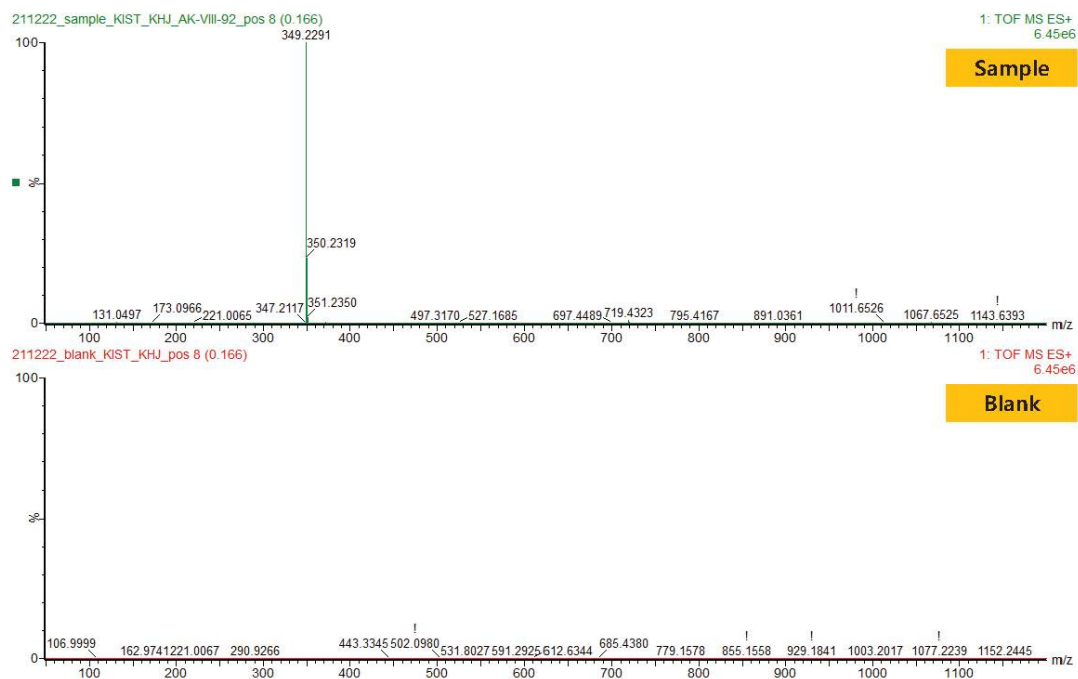
**2e**

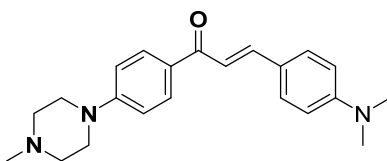
$\text{C}_{23}\text{H}_{29}\text{N}_2\text{O}$   $[\text{M}+\text{H}]^+$ :

Calculated: 349.2280

Found: 349.2291

### Mass Spectrum: AK-VIII-92 (Positive mode)





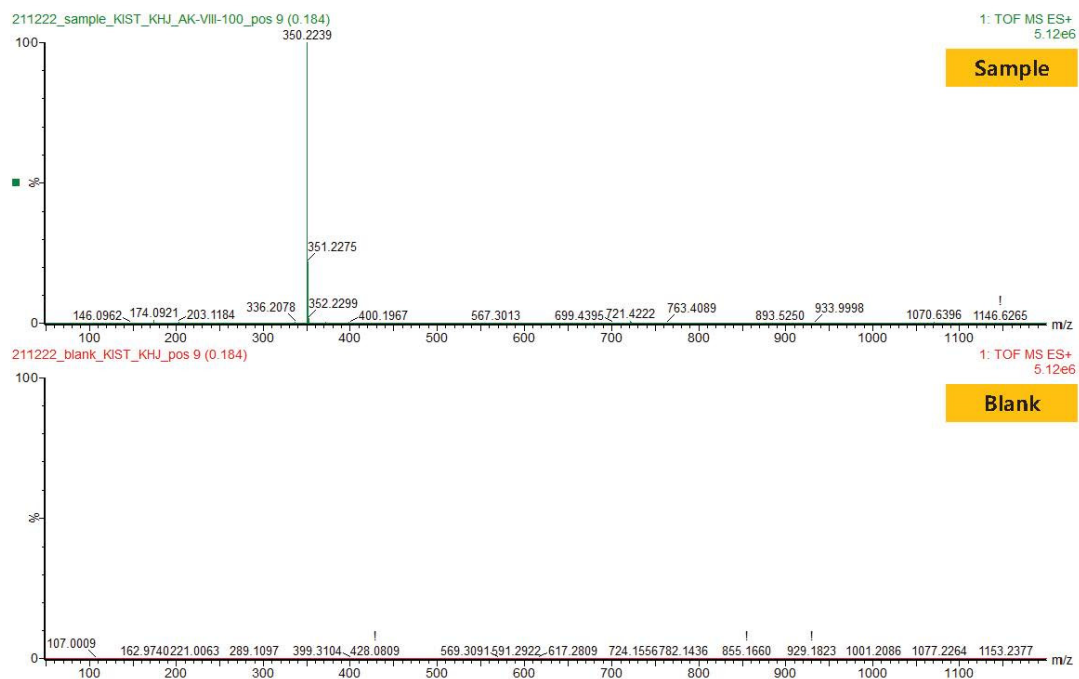
**2f**

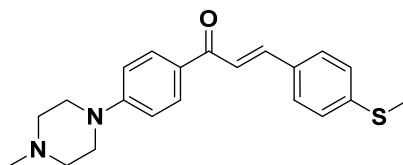
$\text{C}_{22}\text{H}_{28}\text{N}_3\text{O}$   $[\text{M}+\text{H}]^+$ :

Calculated: 350.2232

Found: 350.2239

### Mass Spectrum: AK-VIII-100 (Positive mode)





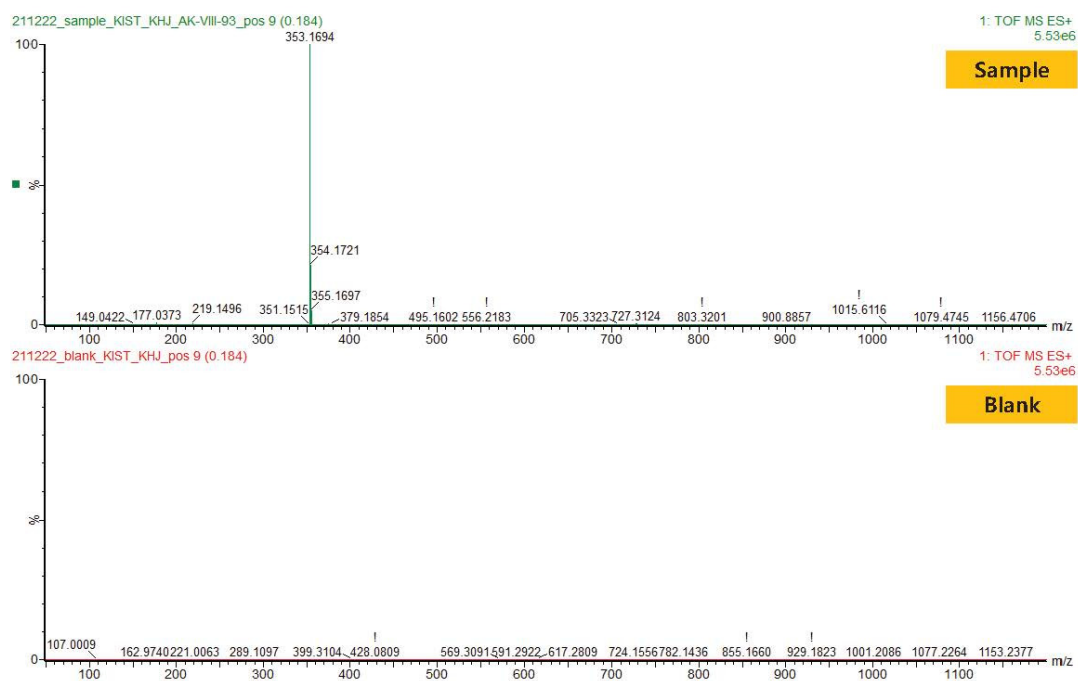
**2g**

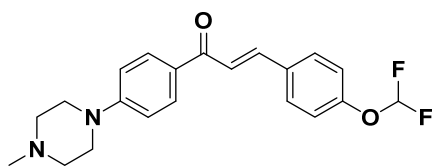
$\text{C}_{21}\text{H}_{25}\text{N}_2\text{OS}$   $[\text{M}+\text{H}]^+$ :

Calculated: 353.1688

Found: 353.1694

### Mass Spectrum: AK-VIII-93 (Positive mode)





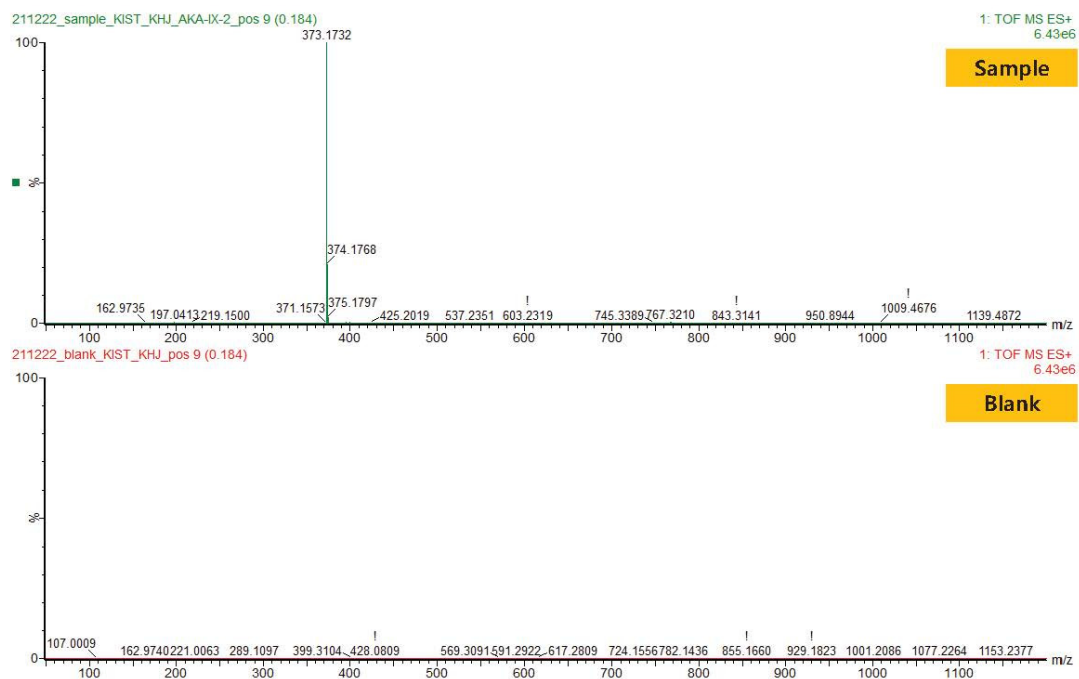
**2h**

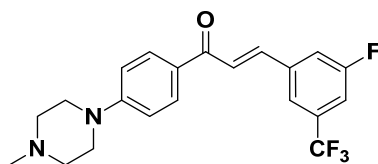
$\text{C}_{21}\text{H}_{23}\text{F}_2\text{N}_2\text{O}_2$   $[\text{M}+\text{H}]^+$ :

Calculated: 373.1728

Found: 373.1732

### Mass Spectrum: AKA-IX-2 (Positive mode)





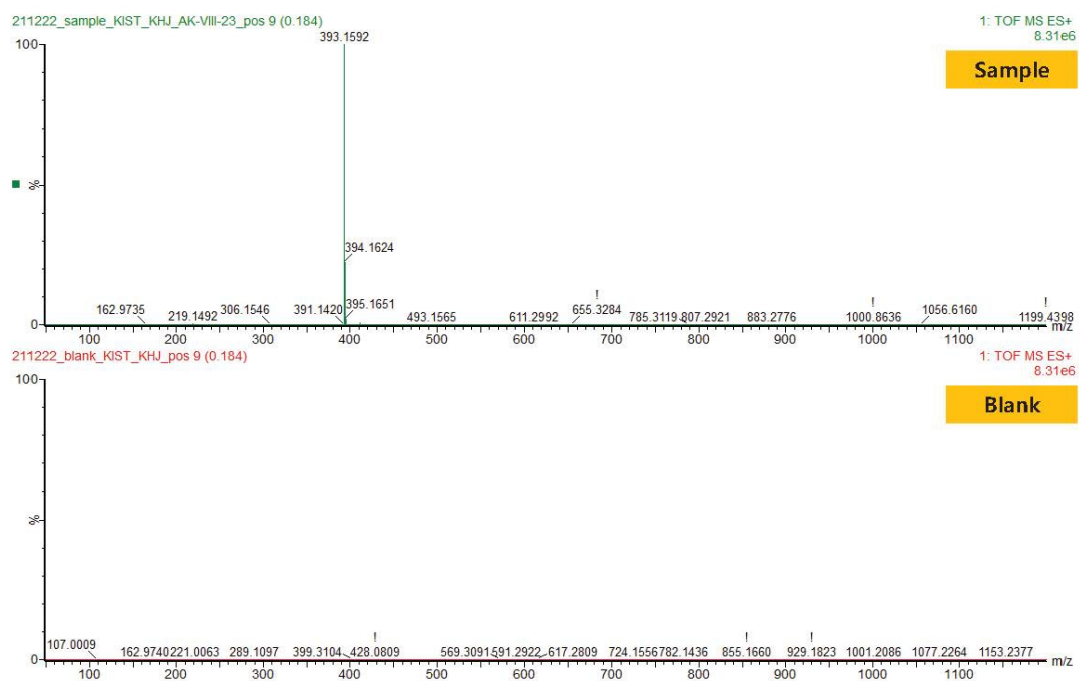
**2i**

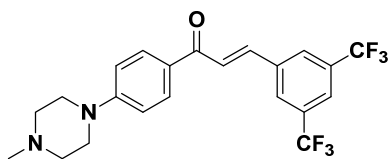
$\text{C}_{21}\text{H}_{21}\text{F}_4\text{N}_2\text{O}$   $[\text{M}+\text{H}]^+$ :

Calculated: 393.1590

Found: 393.1592

### Mass Spectrum: AK-VIII-23 (Positive mode)





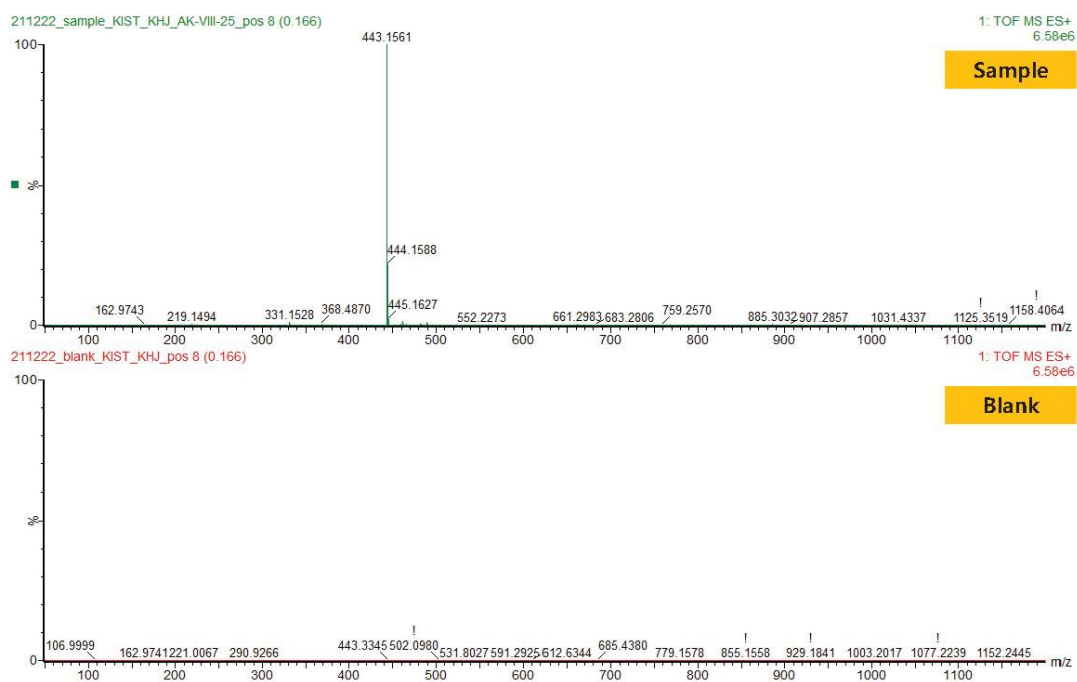
2j

$C_{22}H_{21}F_6N_2O [M+H]^+$

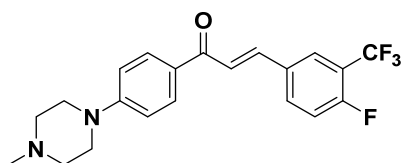
Calculated: 443.1558

Found: 443.1561

### Mass Spectrum: AK-VIII-25 (Positive mode)







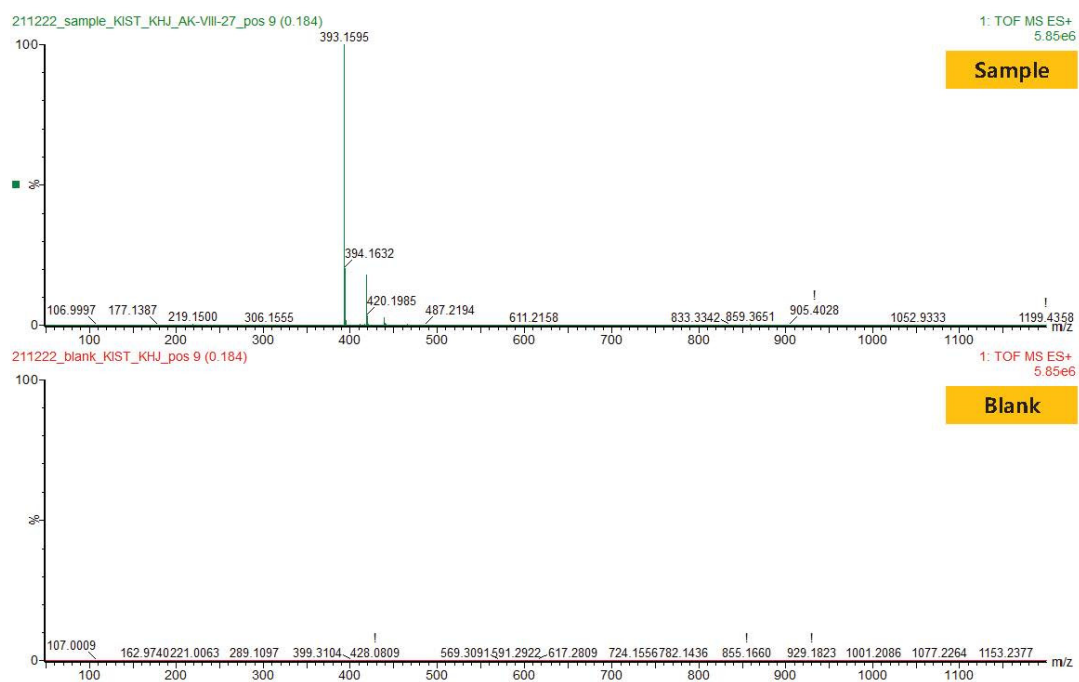
**2k**

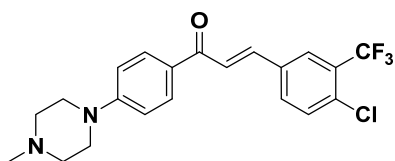
$\text{C}_{21}\text{H}_{21}\text{F}_4\text{N}_2\text{O} [\text{M}+\text{H}]^+$

Calculated: 393.1590

Found: 393.1595

### Mass Spectrum: AK-VIII-27 (Positive mode)





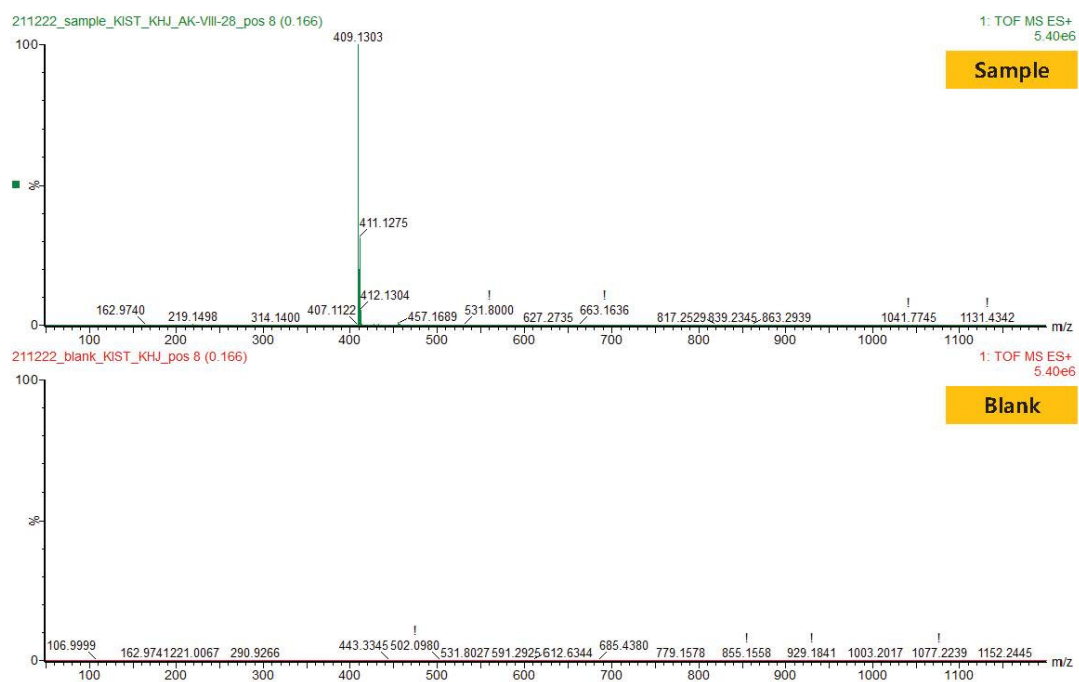
**2I**

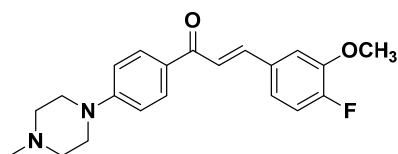
$\text{C}_{21}\text{H}_{21}\text{ClF}_3\text{N}_2\text{O}$   $[\text{M}+\text{H}]^+$ :

Calculated: 409.1295

Found: 409.1303

### Mass Spectrum: AK-VIII-28 (Positive mode)





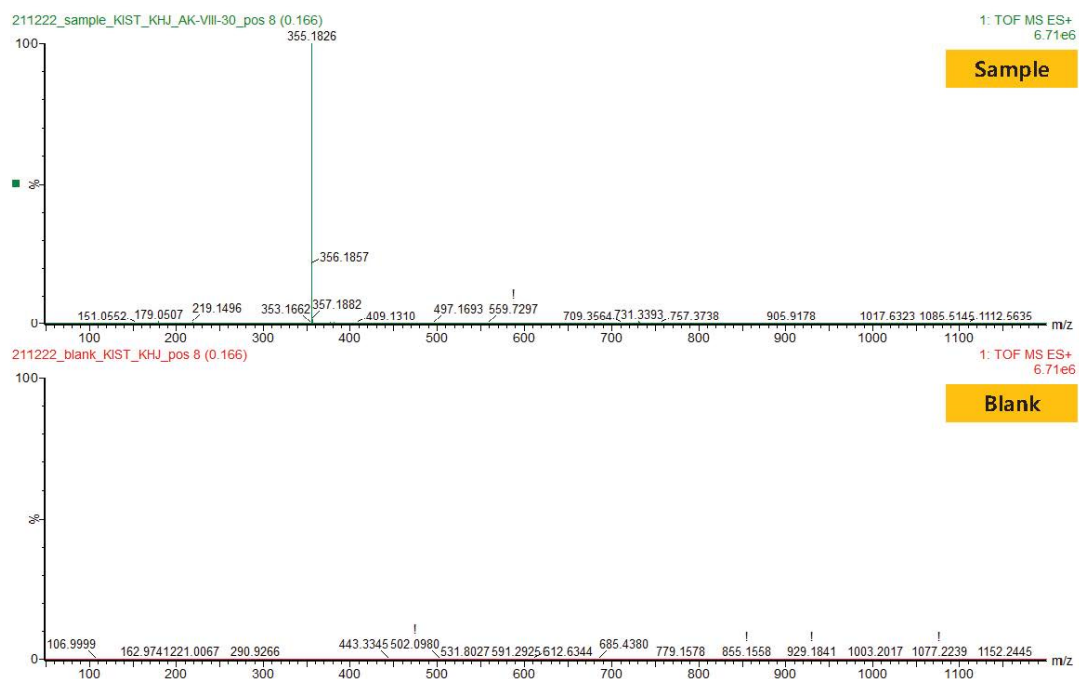
**2m**

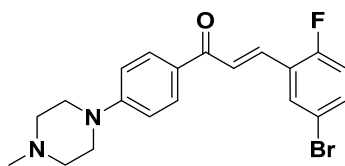
$\text{C}_{21}\text{H}_{24}\text{FN}_2\text{O}_2$   $[\text{M}+\text{H}]^+$ :

Calculated: 355.1822

Found: 355.1826

### Mass Spectrum: AK-VIII-30 (Positive mode)





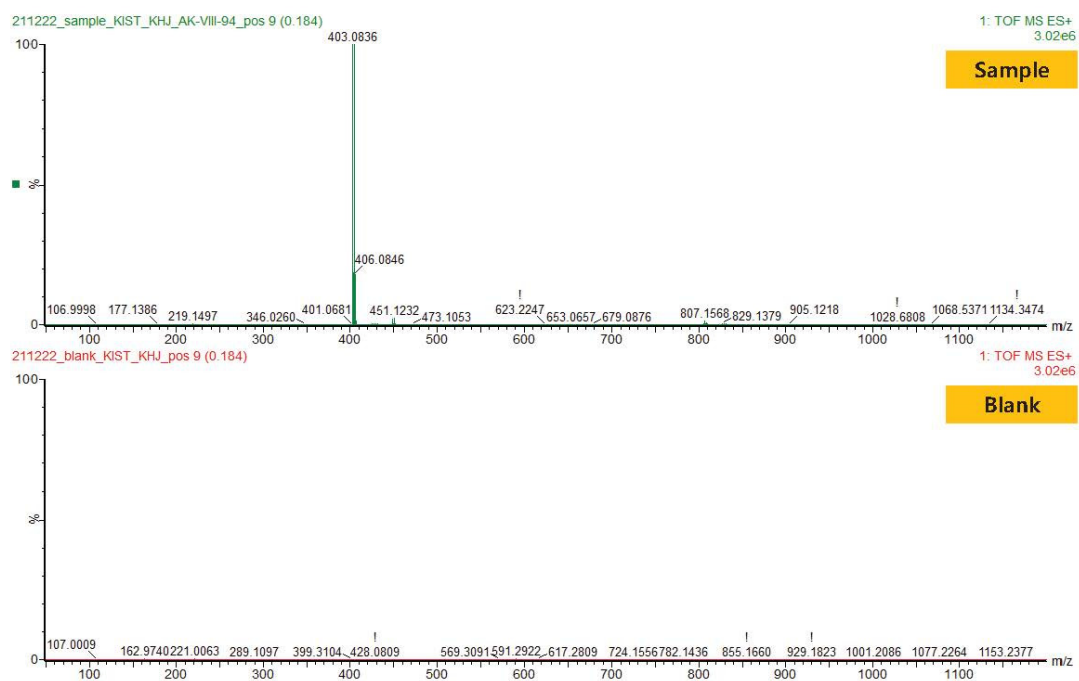
**2n**

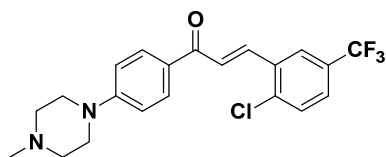
$\text{C}_{20}\text{H}_{21}\text{BrFN}_2\text{O}$   $[\text{M}+\text{H}]^+$ :

Calculated: 403.0821

Found: 403.0836

### Mass Spectrum: AK-VIII-94 (Positive mode)





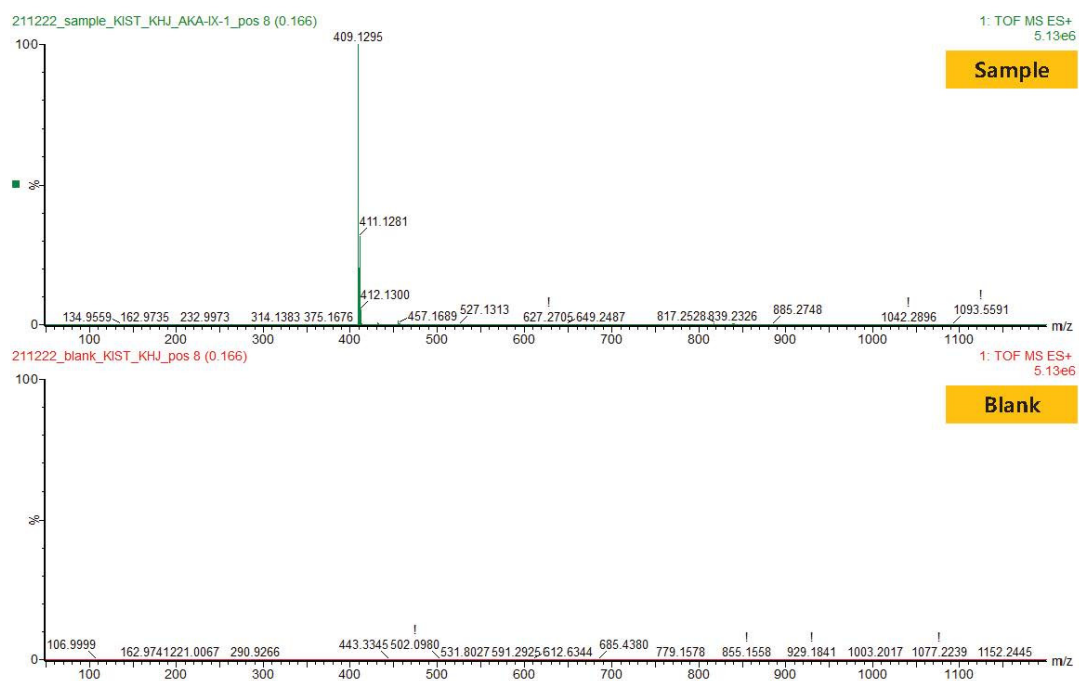
**2o**

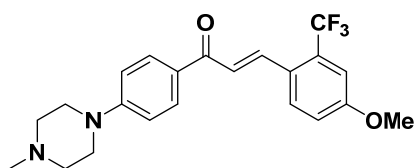
$\text{C}_{21}\text{H}_{21}\text{ClF}_3\text{N}_2\text{O}$   $[\text{M}+\text{H}]^+$ :

Calculated: 409.1295

Found: 409.1295

### Mass Spectrum: AKA-IX-1 (Positive mode)





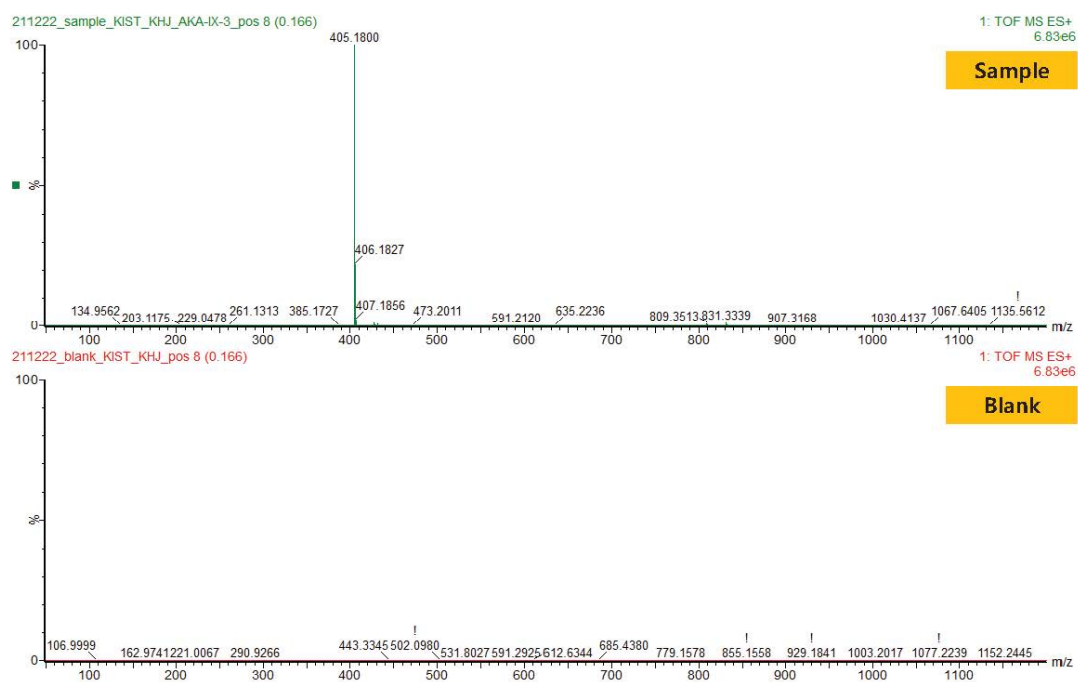
**2p**

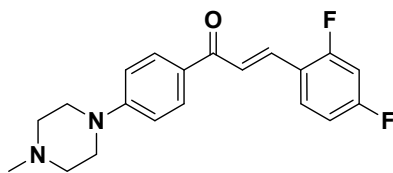
$\text{C}_{22}\text{H}_{24}\text{F}_3\text{N}_2\text{O}_2$   $[\text{M}+\text{H}]^+$ :

Calculated: 405.1790

Found: 405.1800

### Mass Spectrum: AKA-IX-3 (Positive mode)





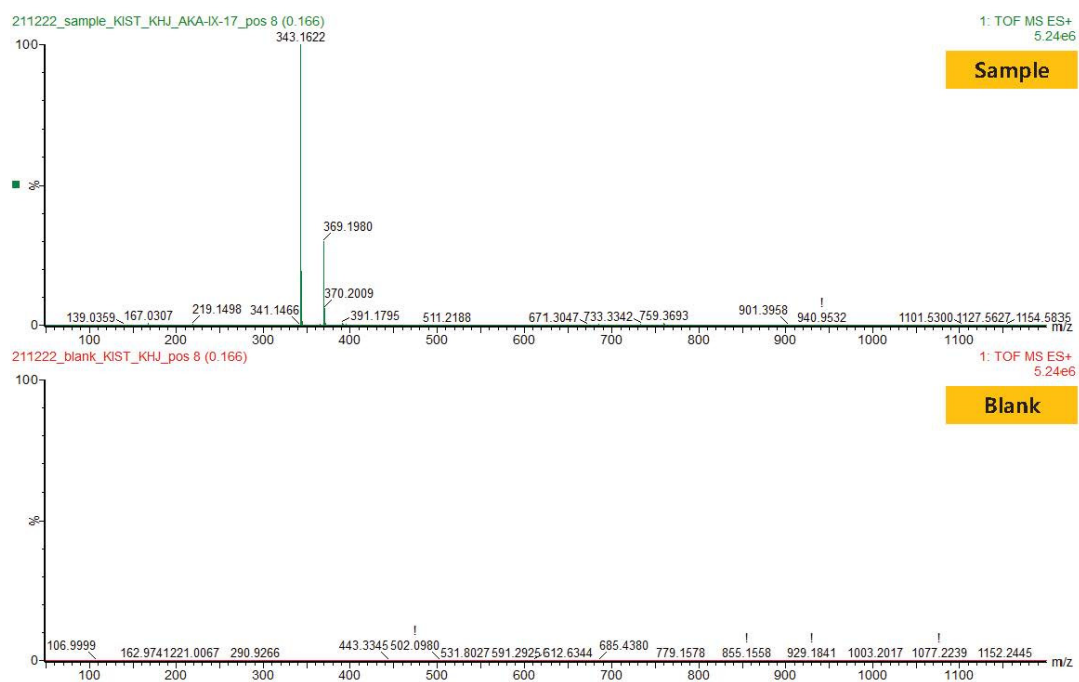
**2q**

$\text{C}_{20}\text{H}_{21}\text{F}_2\text{N}_2\text{O}$   $[\text{M}+\text{H}]^+$ :

Calculated: 343.1622

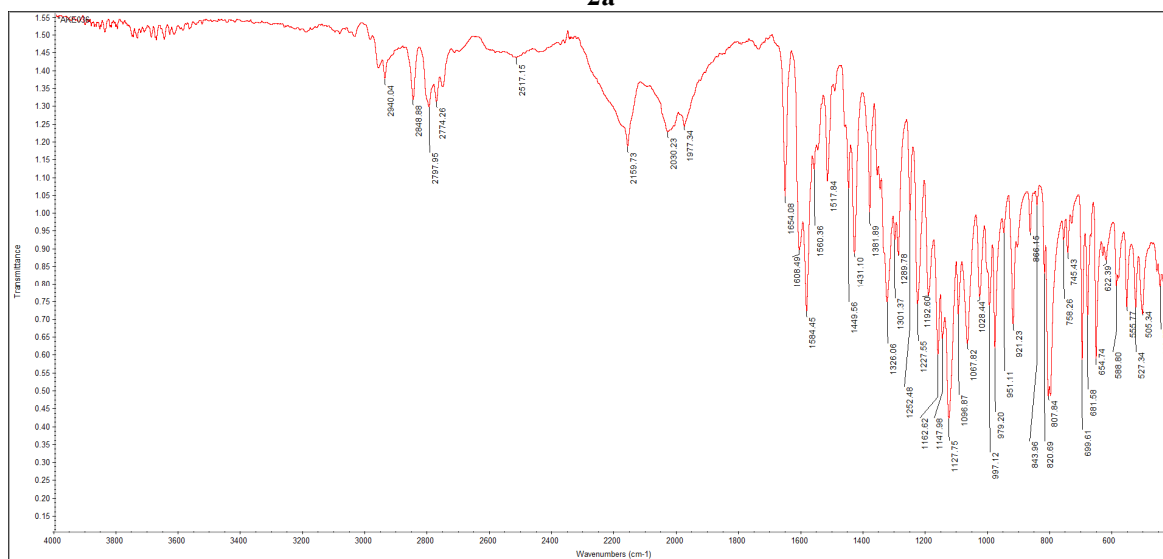
Found: 343.1622

### Mass Spectrum: AKA-IX-17 (Positive mode)

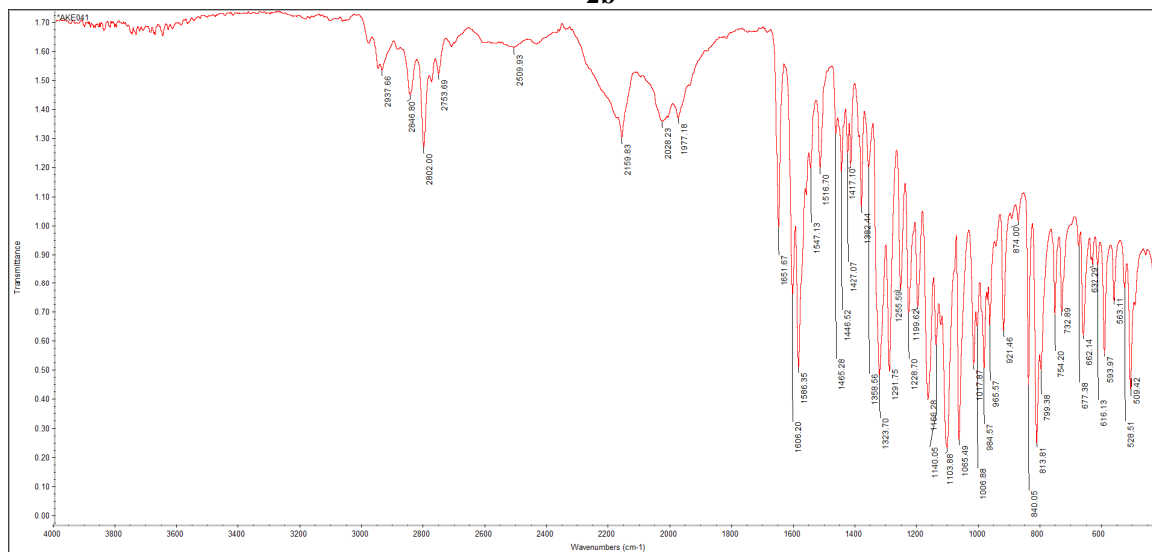


**Figure S3. IR spectra**

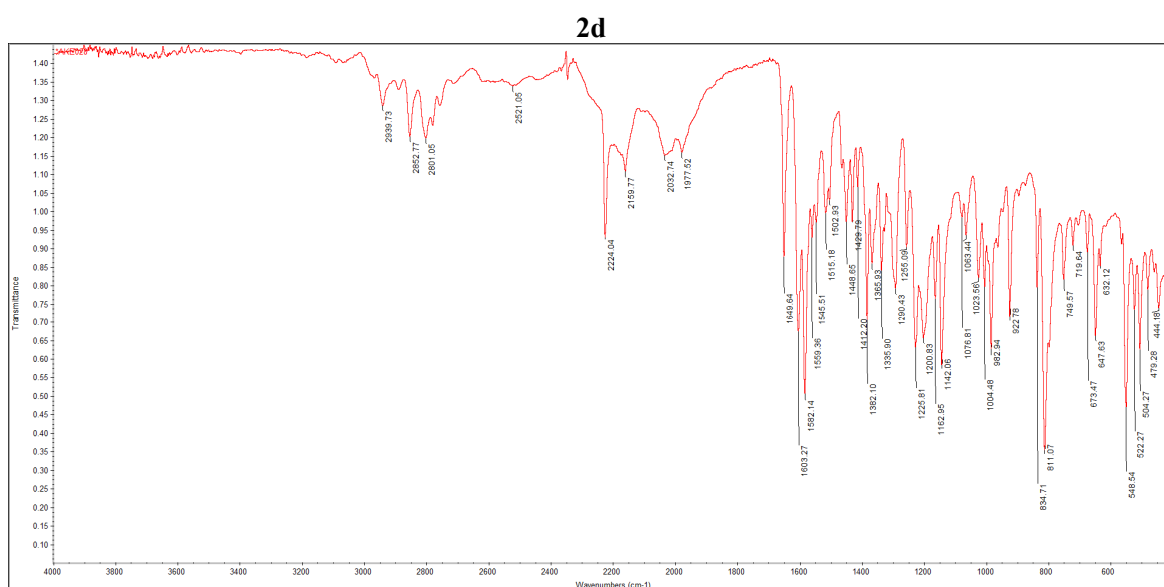
**2a**



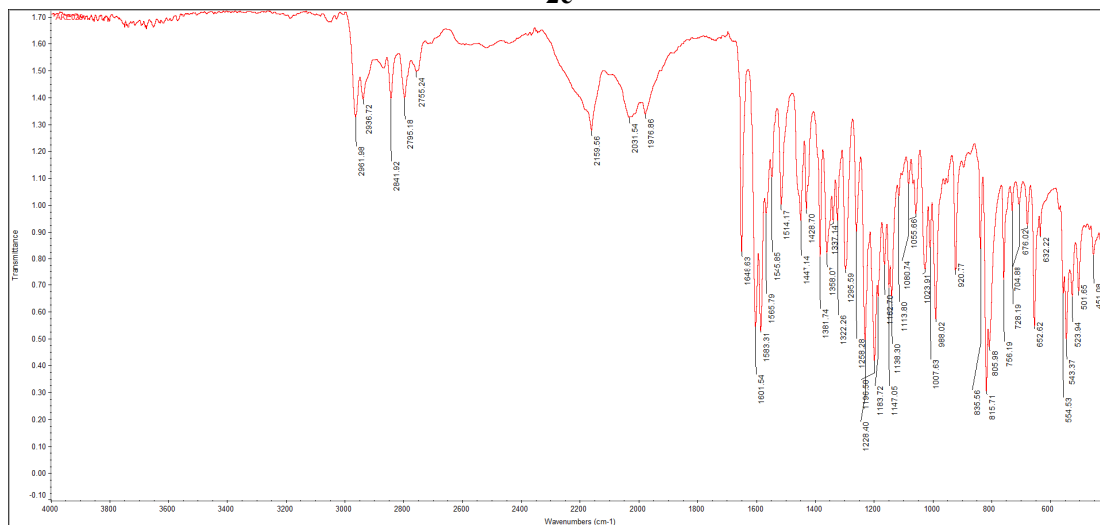
**2b**



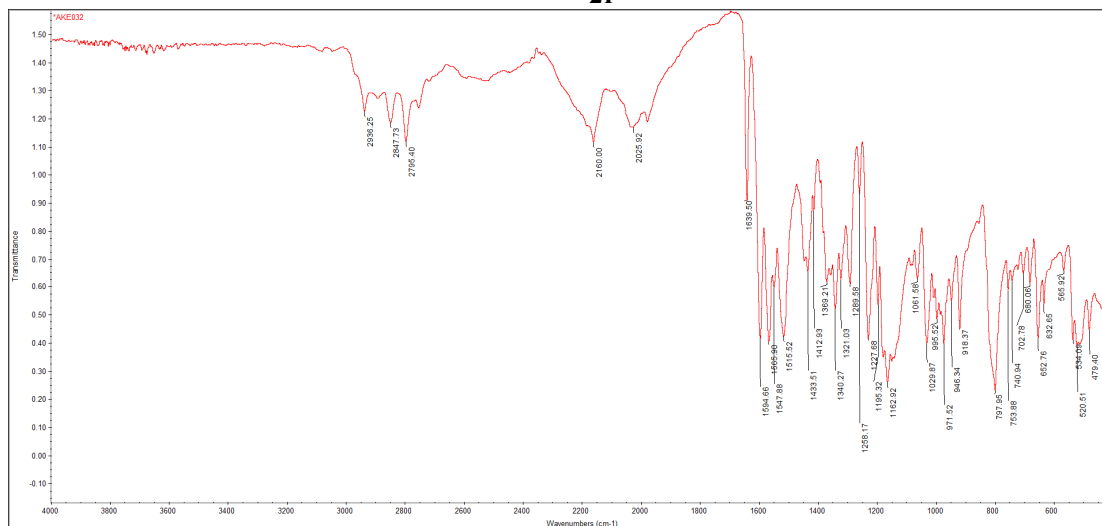




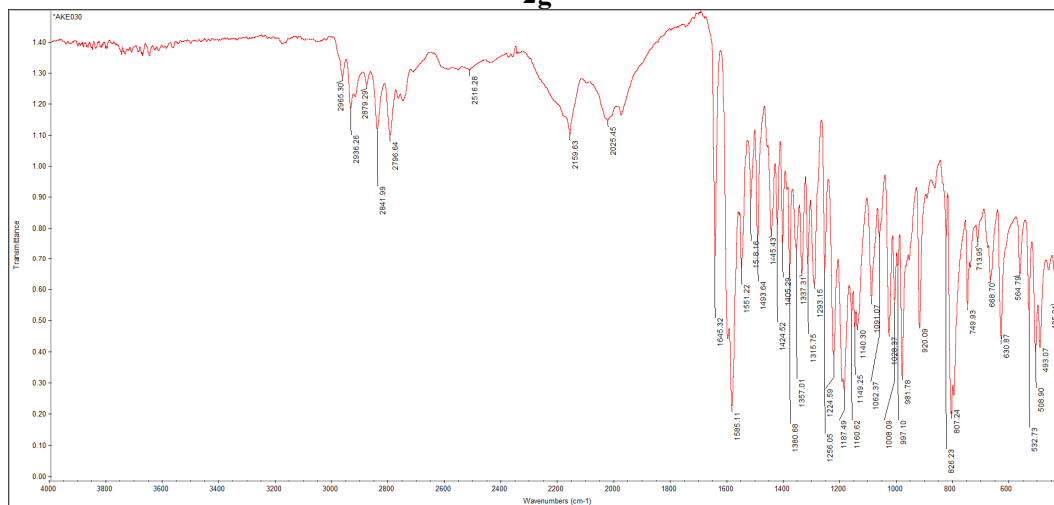
2e



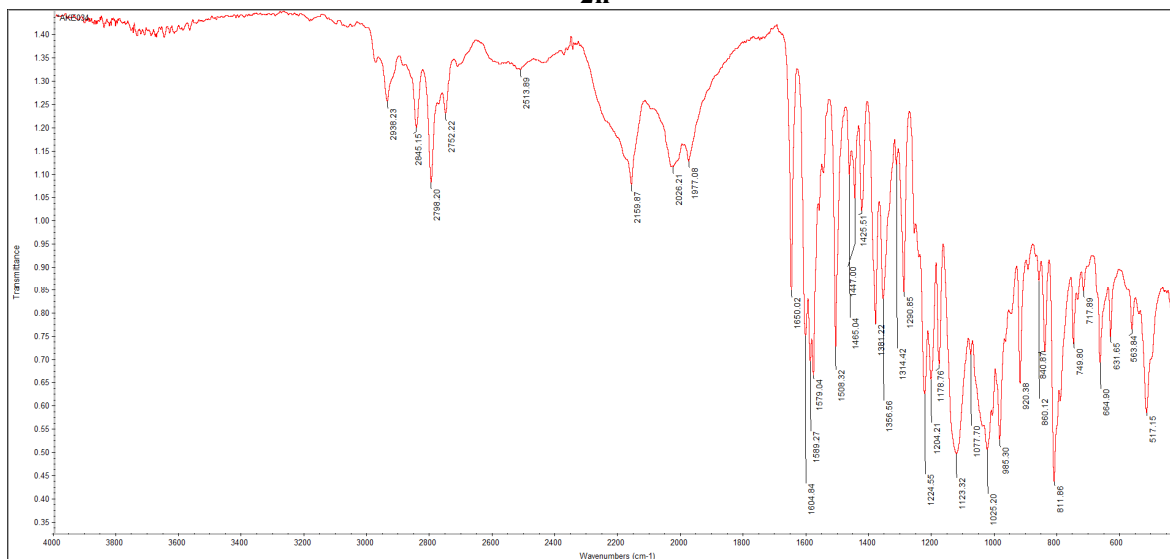
2f



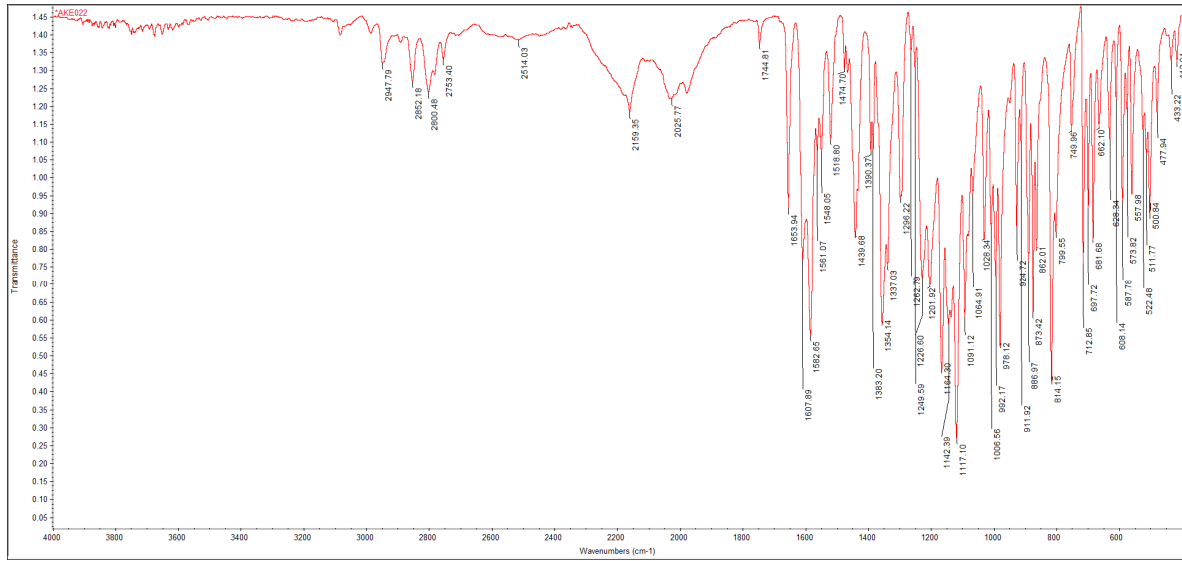
2g



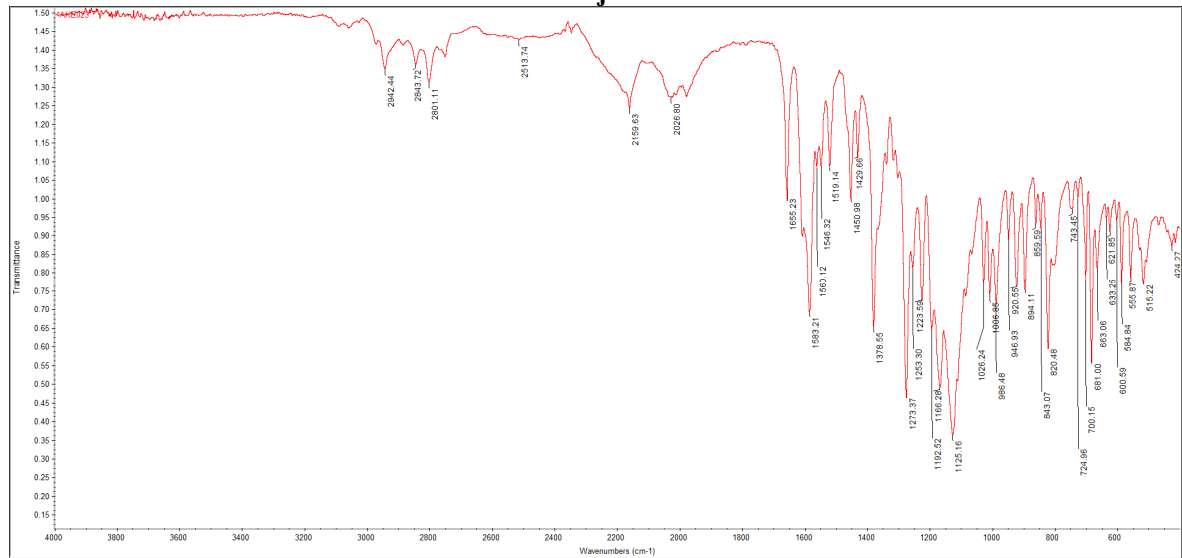
2h



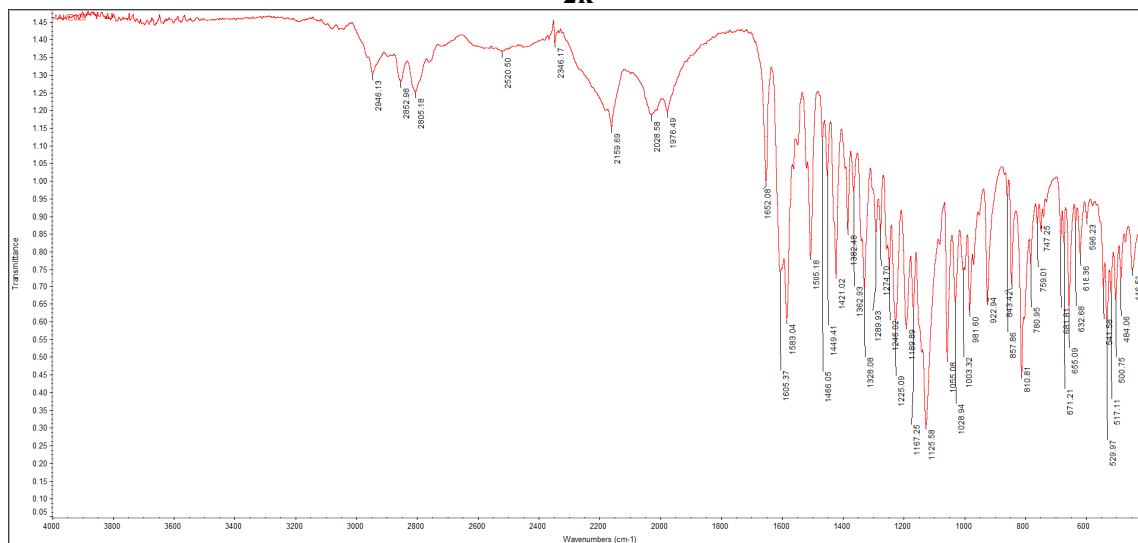
2i



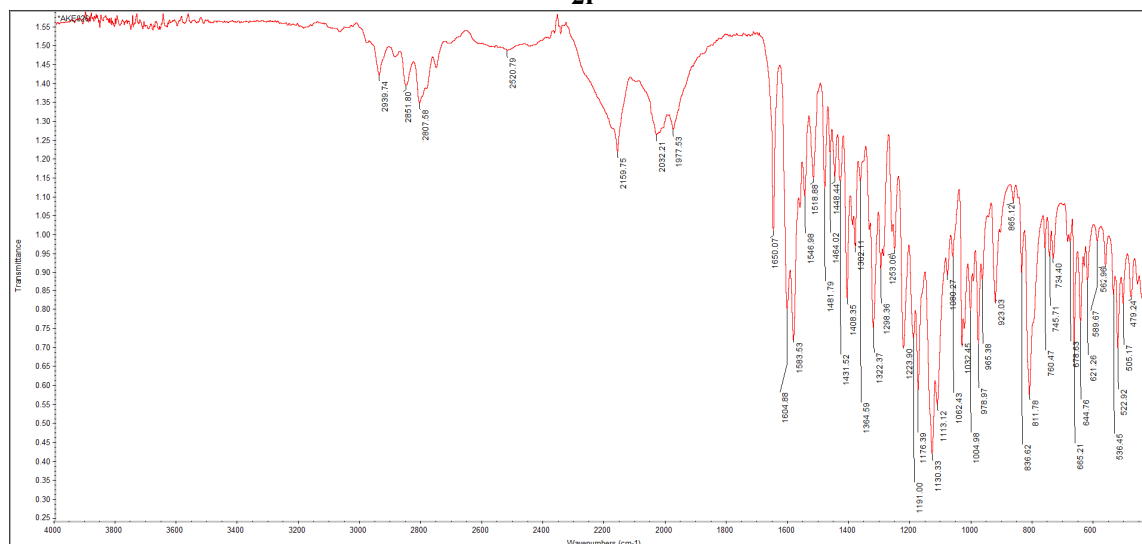
2j

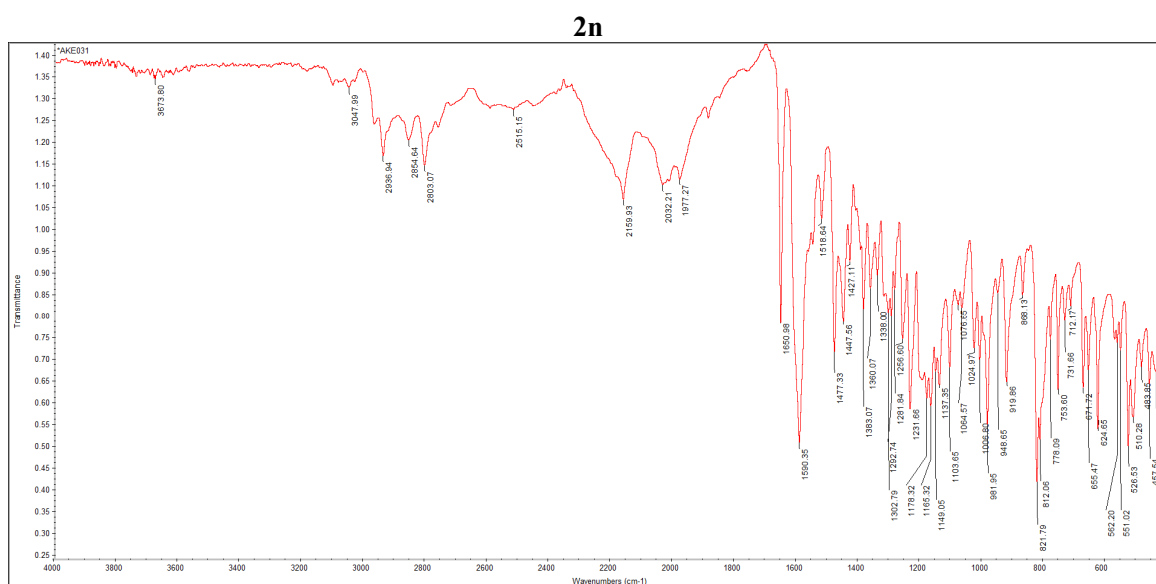
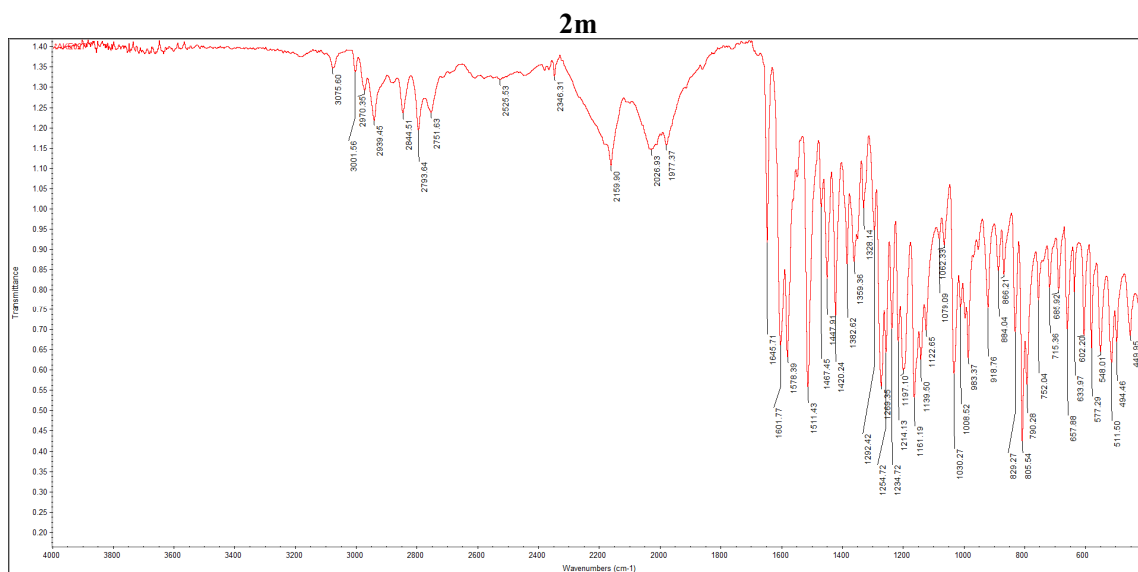


2k

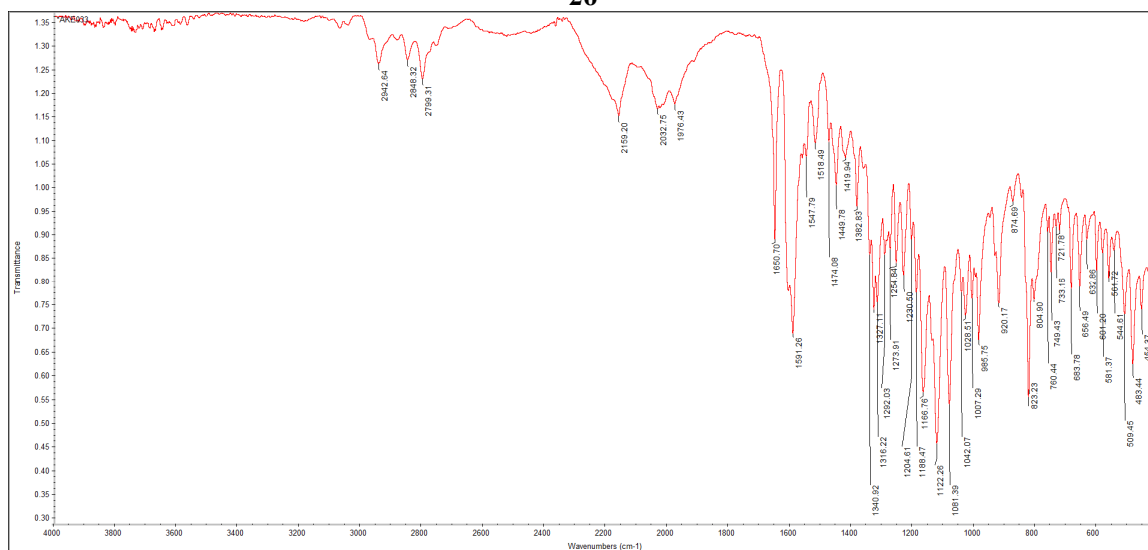


2l

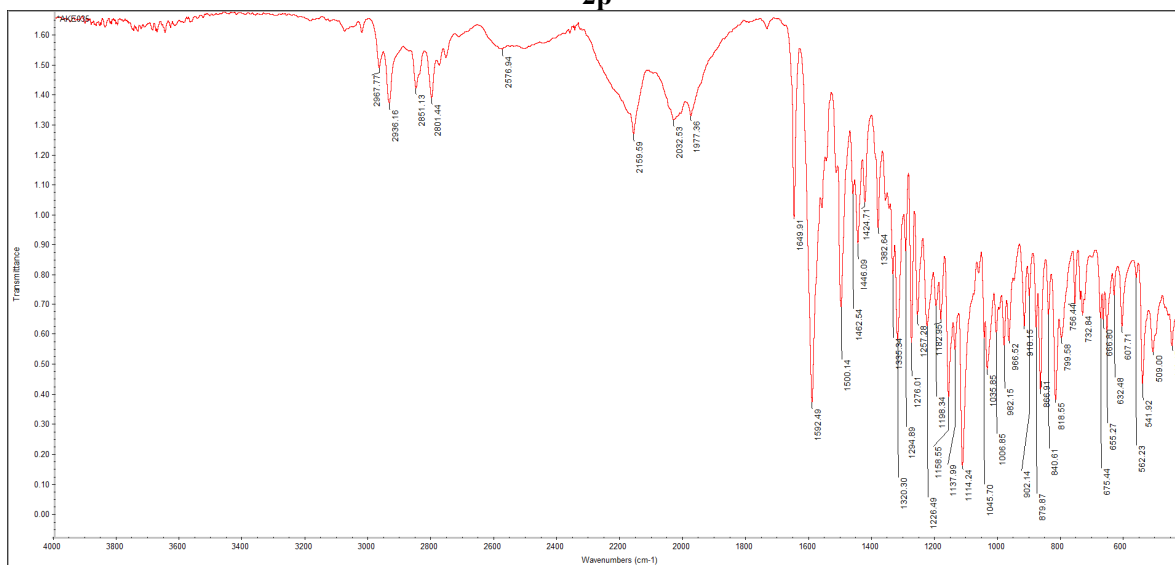




2o



2p

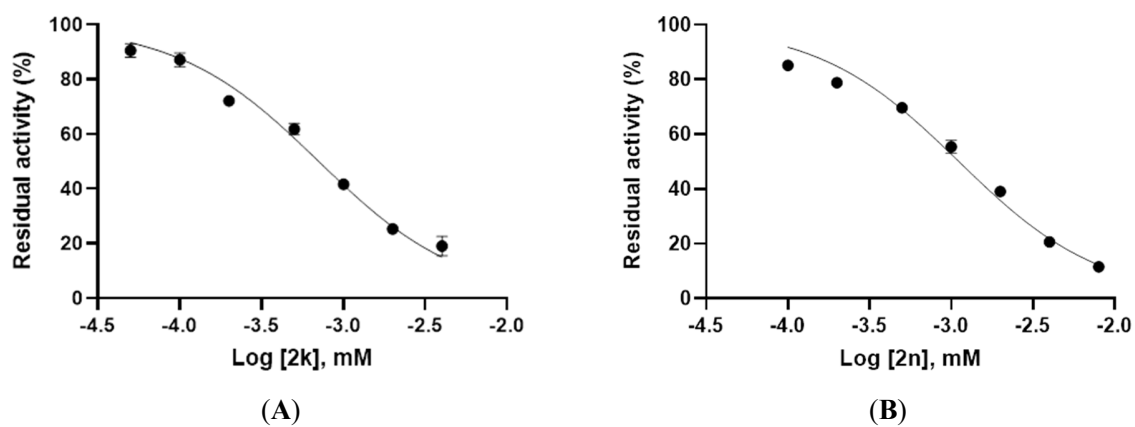


2q





**Figure S4.** IC<sub>50</sub> curves of **2k** and **2n** against MAO-B



**Figure S4.** The IC<sub>50</sub> curves of **2k** (A) and **2n** (B) using GraphPad Prism version 9.3.1. The IC<sub>50</sub> of **2k** and **2n** were determined with 0.71 and 1.11  $\mu$ M, respectively.